Physical Activity Guidelines Advisory Committee Report, 2008

To the Secretary of
Health and Human Services

U.S. Department of Health and Human Services

The findings of this report are those of the Physical Activity Guidelines Advisory Committee. They do not necessarily reflect the views of the Office of Disease Prevention and Health Promotion or the U.S. Department of Health and Human Services.

Suggested citation: Physical Activity Guidelines Advisory Committee. *Physical Activity Guidelines Advisory Committee Report, 2008*. Washington, DC: U.S. Department of Health and Human Services, 2008.

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Prepublication Copy
Issued June 2008

DEPARTMENT OF HEALTH AND HUMAN SERVICES Office of the Secretary

Assistant Secretary for Health
Office of Public Health and Science
Washington D.C. 20201

May 23, 2008

The Honorable Michael O. Leavitt
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Leavitt,

On behalf of the entire 2008 Physical Activity Guidelines Advisory Committee, we are very pleased to submit the *Physical Activity Guidelines Advisory Committee Report, 2008*.

You charged our committee to "…review existing scientific literature to identify where there is sufficient evidence to develop a comprehensive set of specific physical activity recommendations." The Committee's report documents scientific background and rationale for the 2008 edition of the *Physical Activity Guidelines for Americans.* The Committee also identified areas where further scientific research is needed.

The Committee's review and deliberations clearly demonstrated that sedentary behavior confers substantial health risks throughout the lifespan. The health benefits of being habitually physically active appear to apply to all people regardless of age, sex, race/ethnicity, socioeconomic status, and to many people with physical or cognitive disabilities. The amount and intensity of physical activity needed to achieve many health benefits is well within the capacity of most Americans .and can be performed safely. This report provides the scientific basis for these conclusions and the development of federal physical activity guidelines.

For the entire Committee, we want to thank you for the opportunity to support your Prevention Priority. Over the past twelve months, the Committee members and consultants worked exceptionally long and hard to conduct the extensive scientific review that made this report possible. Despite this task being added to their usual busy schedules, they met tight deadlines, provided insight and education to one another, and unselfishly worked to develop a consensus report. Thus, we wish to thank you for assembling a committee of outstanding professionals who are not only knowledgeable and highly productive but also most pleasant in character.

It is important to emphasize that this report could not have been completed without the outstanding support of all the HHS staff who assisted us throughout the entire process. We are very grateful for their substantial assistance in developing an extensive electronic searchable literature database for use by the Committee and for their excellent logistical and management support in all aspects of the Committee's work. Special recognition goes to RADM Penelope Slade Royall and CAPT Richard Troiano of the Office of Disease Prevention and Health Promotion for their tireless dedication in the coordination, and ultimate completion, of this project. This report greatly benefits from the expert editing provided by Anne Brown Rodgers, who helped us present information that is useful and readable, and from the careful work of Reba Norman, who ensured the completeness and accuracy of the report's extensive reference lists.

Our review documents very strong scientific evidence that physically active people have higher levels of health-related fitness, a lower risk of developing a number of disabling medical conditions, and lower rates of various chronic diseases than people who are inactive. Given Americans' low rates of participation in physical activity and high prevalence of chronic diseases and associated disabilities, this report is particularly timely. It provides the necessary foundation for HHS to proceed to develop *Physical Activity Guidelines for Americans, 2008* and related policy statements. Strong federal guidelines, policies, and programs regarding physical activity should be an essential component of any comprehensive disease prevention and health promotion strategy for Americans. Committee members are committed to the broad dissemination of this report and the ensuing guidelines. Please do not hesitate to contact us or any of the Committee members if we can be of further service.

Sincerely,

[Signed May 23, 2008]
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Part A: Executive Summary

Disease prevention and health promotion are high priority features of President George W. Bush's Healthier US initiative and Secretary of Health and Human Services (HHS) Michael O. Leavitt's Prevention Priority. Getting routine medical screenings, making healthy choices and avoiding risks, eating a nutritious diet, and being physically active are major components of chronic disease prevention. On October 27, 2006, Secretary Leavitt announced plans for the development of Federal *Physical Activity Guidelines for Americans* to be issued in 2008. These Federal guidelines will serve as the benchmark and single, authoritative voice for providing science-based guidance on physical activity, fitness, and health for Americans. In preparation for the development by HHS of these guidelines, an important first step was to conduct a comprehensive review and analysis of the scientific literature on physical activity and health published since 1995. This task was assigned to the Physical Activity Guidelines Advisory Committee (PAGAC).

The Physical Activity Guidelines Advisory Committee

Following the announcement by the HHS Secretary of plans to develop physical activity guidelines, nominations for membership on the PAGAC were solicited through the *Federal Register*. PAGAC members were expected to be respected and published experts in the science of physical activity and its role in health promotion and disease prevention; be familiar with the purpose, communication, and application of Federal guidelines; not be employees of the Federal Government; and be free of any commercial conflicts of interest. In February 2007, the Secretary of HHS appointed 13 members to the PAGAC, including a chair and vice-chair. Secretary Leavitt's charge to the PAGAC was to review existing scientific literature to identify where there is sufficient evidence to develop a comprehensive set of specific physical activity recommendations and identify areas where further scientific research is needed. The intent of HHS is to develop physical activity recommendations for all Americans that will be tailored as necessary for specific subgroups of the population. PAGAC was not to prepare guidelines or policy statements. This report is the result of work by the Committee, consultants to the Committee, and HHS support staff. Names and affiliations of PAGAC members, consultants, and HHS support staff are listed at the beginning of this report.

Initially, the PAGAC formed 9 subcommittees, focused on the 9 health outcomes identified by the CDC team assigned to assist the PAGAC: all-cause mortality, cardiorespiratory health, metabolic health, energy balance, musculoskeletal health, functional health, cancer, mental health, and adverse events. PAGAC members then added 2 other subcommittees:

youth and understudied populations (i.e., populations not covered in other chapters — persons with disabilities, women during pregnancy and the postpartum period, and races and ethnicities other than non-Hispanic white). The conclusions in this report represent the consensus of the entire PAGAC.

Report Contents

This report includes 3 major components. The first provides an introduction to the PAGAC process; definition of key terms used in the report; background information on dose response, recent trends in physical activity among Americans, and an overview of physical activity guidelines development in the United States; a summary and integration of the science reviewed by PAGAC; and an explanation of the development and use of the *Physical Activity Guidelines for Americans* Scientific Database. The second component includes 11 sections that review and summarize the scientific literature relating physical activity to individual health outcomes. The third component provides a summary of the PAGAC's collective recommendations for future research. References cited are at the end of each section.

Review of the Science on Physical Activity and Health

One of the PAGAC's major goals was to integrate the scientific information on the relation between physical activity and health and to summarize it in a manner that could be used effectively by HHS personnel to develop the *Physical Activity Guidelines for Americans* and related policy statements. The resulting consensus statements based on the evidence relating physical activity to health are provided in ***Part E: Integration and Summary of the Science*** and the conclusions in each of the chapters in ***Part G: The Science Base***. A number of the key conclusions by the PAGAC, based on their review of the scientific literature, are summarized below.

Overall Benefits of Physical Activity on Health

Very strong scientific evidence based on a wide range of well-conducted studies shows that physically active people have higher levels of health-related fitness, a lower risk profile for developing a number of disabling medical conditions, and lower rates of various chronic diseases than do people who are inactive.

Children and Youth

Strong evidence demonstrates that the physical fitness and health status of children and youth are substantially enhanced by frequent physical activity. Compared to inactive young people, physically active children and youth have higher levels of cardiorespiratory endurance and muscular strength, and well-documented health benefits include reduced body fatness, more favorable cardiovascular and metabolic disease risk profiles, enhanced bone health, and reduced symptoms of anxiety and depression.

Adults and Older Adults

Strong evidence demonstrates that, compared to less active persons, more active men and women have lower rates of all-cause mortality, coronary heart disease, high blood pressure, stroke, type 2 diabetes, metabolic syndrome, colon cancer, breast cancer, and depression. Strong evidence also supports the conclusion that, compared to less active people, physically active adults and older adults exhibit a higher level of cardiorespiratory and muscular fitness, have a healthier body mass and composition, and a biomarker profile that is more favorable for preventing cardiovascular disease and type 2 diabetes and for enhancing bone health. Modest evidence indicates that physically active adults and older adults have better quality sleep and health-related quality of life.

Older Adults

In addition to those benefits listed above, strong evidence indicates that being physically active is associated with higher levels of functional health, a lower risk of falling, and better cognitive function.

Women During Pregnancy and the Postpartum Period

Strong evidence indicates that moderate-intensity physical activity during pregnancy by generally healthy women increases cardiorespiratory and metabolic fitness without increasing the risk of low birth weight, preterm delivery, or early pregnancy loss. Moderate-intensity physical activity during the postpartum period does not appear to adversely affect milk volume or composition or infant growth. Physical activity alone does not produce weight loss in postpartum women except when combined with dietary changes.

Persons With Disabilities

For many physical and cognitive disabilities, scientific evidence for various health and fitness outcomes is still limited due to the lack of research. Moderate to strong evidence indicates that increases in aerobic exercise improve cardiorespiratory fitness in individuals with lower limb loss, multiple sclerosis, stroke, spinal cord injury, and mental illness. Limited data show similar results for people with cerebral palsy, muscular dystrophy, and Alzheimer’s disease. Moderate to strong evidence also exists for improvements in walking speed and walking distance in patients with stroke, multiple sclerosis, and intellectual disabilities. Moderately strong evidence indicates that resistance exercise training improves muscular strength in persons with such conditions as stroke, multiple sclerosis, cerebral palsy, spinal cord injury, and intellectual disability. Although evidence of benefit is suggestive for such outcomes as flexibility, atherogenic lipids, bone mineral density, and quality of life, the data are still very limited.

Racial and Ethnic Diversity

Only a limited number of prospective observational or experimental studies investigating the relation between physical activity and health outcomes have had adequate samples of non-Hispanic white men or women and one or more other race/ethnicities to allow a direct comparison of benefits. However, in the few studies where direct comparisons have been made, no meaningful difference appears to exist, and studies conducted in other countries with race-ethnic populations other than non-Hispanic white report similar results. Thus, based on the currently available scientific evidence, the dose of physical activity that provides various favorable health and fitness outcomes appears to be similar for adults of various races and ethnicities.

Persons Who Are Overweight or Obese

Strong evidence shows that physically active adults who are overweight or obese experience a variety of health benefits that are generally similar to those observed in people of optimal body weight (body mass index [BMI] = 18.5-24.9). These benefits include lower rates of all-cause mortality, coronary heart disease, hypertension, stroke, type 2 diabetes, colon cancer, and breast cancer. Some of these benefits appear to be independent of a loss in body weight, while in some cases weight loss in conjunction with an increase in physical activity results in even greater benefits. Because of the health benefits of physical activity that are independent of body weight classification, adults of all sizes and shapes gain health and fitness benefits by being habitually physically active.

Patterns of Physical Activity Associated With Better Health and Fitness

PAGAC members recognized that, when considering the intensity of an activity, it is most appropriate scientifically to express the intensity relative to a person's capacity (relative intensity). However, the PAGAC also recognized that communicating to the public the process of determining relative intensity is difficult and that intensity expressed in absolute terms is a reasonable alternative. Table D.1 and Figure D.1 located in ***Part D: Background*** provide information on the relation between absolute and relative intensity. Also, the committee concluded that, when classifying activities by intensity using metabolic equivalents (METs), the appropriate classification of moderate-intensity activity is 3.0 to 5.9 rather than 3.0 to 6.0 METs and vigorous intensity is 6.0 or greater METs (Table D.2).

Based on the existing science, it is not possible to be highly precise in selecting a single expression of activity amount that provides improved health because of the diversity in the types of physical activity reported and the conditions under which they are performed, the different questionnaires used to assess these activities, and the various units of measurement used to express the characteristics of the activity. Also, the baseline activity and fitness levels of the population and the targeted health outcomes influence the effective dose. The committee constructed a table to assist in translating the different units of measurements for the amount of activity performed for a range of activity intensities performed for 150 and 300 minutes per week (2.5 and 5 hours per week) (Table D.3).

Children and Youth

Few studies have provided data on the dose response for various health and fitness outcomes in children and youth. However, substantial data indicate that important health and fitness benefits can be expected to accrue to most children and youth who participate daily in 60 or more minutes of moderate to vigorous physical activity. Certain specific types of physical activity should be included in an overall physical activity pattern in order for children and youth to gain comprehensive health benefits. These include regular participation in each of the following types of physical activity on 3 or more days per week: resistance exercise to enhance muscular strength in the large muscle groups of the trunk and limbs, vigorous aerobic exercise to improve cardiorespiratory fitness and cardiovascular and metabolic disease risk factors, and weight-loading activities to promote bone health. Experiences consistent with these goals involve participation in physical activities that are developmentally appropriate, that minimize the potential risks of overtraining and injuries, and that provide children and youth with opportunities for enjoyable participation in a wide range of specific forms of physical activity.

Adults and Older Adults

Data from a large number of studies evaluating a wide variety of benefits in diverse populations generally support 30 to 60 minutes per day of moderate to vigorous intensity physical activity on 5 or more days of the week. For a number of benefits, such as lower risk for all-cause mortality, coronary heart disease, stroke, hypertension, and type 2 diabetes in adults and older adults, lower risk is consistently observed at 2.5 hours per week (equivalent to 30 minutes per day, 5 days per week) of moderate to vigorous intensity activity. The amount of moderate to vigorous intensity activity most consistently associated with significantly lower rates of colon and breast cancer and the prevention of unhealthy weight gain or significant weight loss by physical activity alone is in the range of 3 to 5 hours per week.

It is possible to combine aerobic activities of different types and intensities into a single measure of amount of activity. For many studies, the amount of moderate and vigorous intensity activity associated with significantly lower rates of disease or improvements in biomarkers and fitness is in the range of 500 to 1,000 MET-minutes per week. An adult can achieve a target of 500 MET-minutes per week by walking at about 3.0 miles per hour for approximately 150 minutes per week (7.5 miles), walking faster at 4.0 miles per hour for 100 minutes (6.6 miles), or jogging or running at 6 miles per hour for about 50 minutes per week (5.0 miles). To achieve 1,000 MET-minutes per week, these amounts of activity would need to be doubled. For an explanation of the use of METs and MET-minutes for calculating the amount of activity see ***Part D: Background***, especially Table D.2 and its associated text.

Resistance or muscle-strengthening exercises are important for maintaining muscle and bone health, and these exercises enhance functional status and contribute to a reduction of falls in older adults. Most of the evidence supports a resistance activity program with the following characteristics: progressive muscle strengthening exercises that target all major muscle groups performed on 2 or more days per week. To enhance muscle strength, 8 to 12 repetitions of each exercise should be performed to volitional fatigue. One set is effective; however, limited evidence suggests that 2 or 3 sets may be more effective.

Older Adults

If a person has a low exercise capacity (physical fitness), the intensity and amount of activity needed to achieve many health-related and fitness benefits are less than for someone who has a higher level of activity and fitness. Because the exercise capacity of adults tends to decrease as they age, older adults generally have lower exercise capacities than younger persons. Thus, they need a physical activity plan that is of lower absolute intensity and amount (but similar in relative intensity and amount) than is appropriate for more fit people, especially when they have been sedentary and are starting an activity program.

Older Adults at Risk of Falls

For older adults at risk of falling, strong evidence exists that regular physical activity is safe and reduces falls by about 30%. Most evidence supports a program of exercise with the following characteristics: 3 times per week of balance training and moderate-intensity muscle-strengthening activities for 30 minutes per session, with additional encouragement to participate in moderate-intensity walking activities 2 or more times per week for 30 minutes per session. Some evidence, albeit less consistent, suggests that tai chi exercises also reduce falls. There is no evidence that planned physical activity reduces falls in adults and older adults who are not at risk of falls.

Persons With Disabilities

For a majority of the studies reviewed involving persons with disabilities, the exercise regimen followed was that currently recommended for the general public — aerobic exercise of 30 to 60 minutes, 3 to 5 days per week at moderate intensity, and resistance training with 1 or 2 sets of 8 to 12 repetitions using appropriate muscle groups 2 to 3 times per week. Although other activity regimens might be effective, they have not been adequately evaluated.

Persons Achieving Weight Stability

The optimal amount of physical activity needed for weight maintenance (defined as less than 3% change in body weight) over the long-term is unclear. However, the evidence is clear that physical activity provides benefit for weight stability. A great deal of inter-individual variability exists with physical activity and weight stability, and many persons may need more than 150 minutes of moderate-intensity activity per week to maintain their weight at a stable level. Data from recent well-designed randomized controlled trials lasting up to 12 months indicate that aerobic physical activity performed to achieve 13 to 26 MET-hours per week is associated with approximately a 1% to 3% weight loss (i.e., an amount generally considered to represent weight stability). Thirteen MET-hours per week is approximately equivalent to walking at 4 miles per hour for 150 minutes per week or jogging at 6 miles per hour for 75 minutes per week.

Persons Achieving Weight Loss

A wide range of studies provides evidence of a dose-response relation between physical activity and weight loss. Clear, consistent data show that a large volume of physical activity is needed for weight loss in the absence of concurrent dietary changes. The physical activity equivalent of 26 kilocalories per kilogram of body weight (1,560 MET-minutes) or more per week is needed for weight loss of 5% or greater. Smaller amounts of weight loss are seen with smaller amounts of physical activity. This relatively high volume of physical activity is equivalent to walking about 45 minutes per day at 4 miles per hour or about 70 minutes per day at 3 miles per hour, or jogging 22 minutes per day at 6 miles per hour.

The role of energy intake (diet) must be considered in any discussion of weight control. When calorie intake is carefully controlled at a baseline level, the magnitude of any weight loss is what would be expected given the energy expenditure of the person's physical activity. However, in situations in which people's dietary intake is not controlled, the amount of weight loss due to the increase in physical activity is not commensurate to what would be expected. Therefore, for most people to achieve substantial weight loss (i.e., more than 5% decrease in body weight), a dietary intervention also is needed. The dietary intervention could include either maintenance of baseline caloric intake, or a reduction in caloric intake to accompany the physical activity intervention. The magnitude of change in weight due to physical activity is additive to that associated with caloric restriction.

Persons Achieving Weight Maintenance After Weight Loss

The scientific evidence for the effectiveness of physical activity alone in preventing weight regain following significant weight loss is limited. Available data indicate that to prevent substantial weight regain over 6 months or longer, many adults need to exercise in the range of 60 minutes of walking or 30 minutes of jogging daily (approximately 4.4 kilocalories per kilogram per day of activity energy expenditure). The literature generally supports the concept that "more is better" for long-term weight maintenance following weight loss. Further, the evidence indicates that individuals who are successful at long-term weight maintenance appear to limit caloric intake in addition to maintaining physical activity.

Special Considerations Related to the Pattern of Physical Activity and Health

The following section presents additional findings from the Committee's review of the literature. These findings represent important considerations for developing comprehensive physical activity guidelines for Americans.

Some Physical Activity Is Better Than None

The least active people in the population generally have the highest risk of a variety of negative health outcomes. Although the minimum amount of physical activity needed to decrease this risk is not clear, increasing evidence suggests that participating in no more than 1 hour per week of moderate-intensity physical activity is associated with lower risk of all-cause mortality and the incidence of coronary heart disease. At this lower amount and intensity of activity, the benefits usually are less than that observed with greater amounts of activity, and studies are much less consistent about the nature and magnitude of these benefits. Nevertheless, the dose-response curves for the major health benefits clearly indicate an inverse relation between the dose of activity and rate of disease. Although the minimum amount of activity needed to produce a benefit cannot be stated with certainty, nothing would suggest a threshold below which there are no benefits.

Additional Health Benefits With More Physical Activity

Reasonably strong evidence demonstrates that participating in moderate to vigorous physical activity for more than 150 minutes per week is associated with greater health benefits for a variety of health outcomes, including chronic disease prevention, improvement of various disease biomarkers, and the maintenance of a healthy weight. However, in a number of studies where such a dose response is observed in preventing chronic disease or reducing all-cause mortality, the relation appears to be curvilinear. This means that the absolute increase in benefits becomes less and less for any given increase in the amount of physical activity.

Additional Benefits With Vigorous Physical Activity

Strong evidence indicates that an increase in intensity is associated with greater improvements for some health outcomes compared to those observed with moderate-intensity activity. This is especially true for outcomes related to fitness. However, it should be noted that an increase in intensity was often associated with an increase in volume of activity for many observational and experimental studies, and it is difficult to separate the benefits of each.

Frequency of Physical Activity

Very limited published research has systematically evaluated health or fitness benefits in response to different frequencies of activity sessions per week when the amount of activity is held reasonably constant. Although the data are limited, the results suggest that for health and fitness benefits, the frequency of activity is much less important than the amount or intensity. Many experimental studies since 1995 have demonstrated beneficial effects of 120 to 150 minutes per week of moderate- or vigorous-intensity activity, usually performed during 3 to 5 sessions per week, so we know that this frequency of activity is effective. Only limited data are available comparing the benefits from just 1 or 2 sessions per week with multiple sessions spread throughout the week with activity amount and intensity held constant.

Accumulation of Physical Activity

The concept of accumulation refers to performing multiple short bouts of physical activity throughout the day. Some scientific evidence of moderate strength suggests that accumulating 30 or more minutes of moderate- to vigorous-intensity aerobic activity throughout the day in bouts of 10 minutes or longer produces improvements in cardiorespiratory fitness. Limited data indicate that accumulated short bouts of 8 to 10 minutes improve selected biomarkers for cardiovascular disease in a manner generally similar to that observed when activity of a similar amount and intensity is performed in a single bout of 30 or more minutes. Data on the effects of accumulating activity involving multiple short bouts for the prevention of major clinical outcomes, such as all-cause mortality, cardiovascular disease, diabetes, and selected cancers, are very limited due to the type of data collected from the questionnaires in most prospective observational studies. In these studies, people are generally asked about the total amount of physical activity performed, and it has not been possible to precisely differentiate between activities conducted in a single, long bout versus those conducted in multiple, short bouts over the day.

Health Benefits of Brisk Walking

Strong evidence shows that a regimen of brisk walking provides a number of health and fitness benefits for adults and older adults, including lower risk of all-cause mortality, cardiovascular disease, and type 2 diabetes. Some evidence is available indicating that walking at faster pace is associated with greater health benefits than walking at a slower pace. Strong evidence also shows that frequent bouts of walking increase cardiorespiratory and metabolic fitness, especially in people who have been performing little activity on a regular basis. Limited to moderate evidence suggests that walking helps to maintain bone density and reduce fractures over time, especially in women, and helps to maintain joint health and functional ability in adults and older adults.

Safety and Adverse Events

Activity-related adverse events such as musculoskeletal injuries are common but are usually mild, especially for moderate intensity activities such as walking. Overall, the health benefits of regular physical activity outweigh the risks. Much of the research that has addressed adverse events during physical activity has evaluated the risk of musculoskeletal injuries or sudden cardiac death during vigorous physical activity (e.g., jogging, running, competitive sports, military training). Few well-conducted studies are available evaluating risk during moderate-intensity activity intended primarily to improve health. Injury rates are higher for collision and contact sports than for activities with fewer and less forceful contact with other people or objects. Walking for exercise, gardening or yard work, dancing, swimming, and golf are activities with the lowest injury rates. Injuries are more likely to happen when people are more physically active than usual, and the risk is related to the size of the increase. A series of small increments in physical activity, each followed by a period of adaptation, is associated with lower rates of musculoskeletal injuries than is an abrupt increase to the same final level. For sudden cardiac adverse events, intensity appears to be more important than frequency or duration. The protective value of a medical consultation for persons with or without chronic diseases who are interested in increasing their physical activity level is not established.

Research Recommendations

Individual chapters in ***Part G: The Science Base*** provide a list of recommendations regarding issues that should receive priorities for future research. The PAGAC felt that it would be valuable to collate the major research recommendations into one section, ***Part H: Research Recommendations,*** and to include some overarching recommendations that pertain to more than one health outcome. For example, it became apparent during the PAGAC's review that various populations are underrepresented in studies on physical activity and health. These populations represent a substantial portion of the population at risk because of their high prevalence of sedentary behavior. They include persons of low socioeconomic status, racial-ethnic minorities, persons with disabilities, and women during pregnancy and the postpartum period. Also, inadequate data are available to answer a number of questions about dose response for a variety of health outcomes, such as the effects of activity intensity, bout duration, or frequency when total amount or volume of activity is held constant. More data are needed to better define both the low and high ends of the dose-response relation for various health outcomes. Additional research on the basic biological mechanisms modified by changes in physical activity will help establish causality for specific clinical outcomes. National surveillance systems also are needed to track trends in total daily activity energy expenditure in various populations throughout the lifespan.

Part B: Introduction

Setting the Stage for Physical Activity Guidelines for Americans

The Department of Health and Human Services (HHS) is entrusted with a leadership position in the nation's government to promote, create, and maintain a healthy America, and the President's HealthierUS Initiative establishes a federal framework for wellness-related activities and programs. In May 2006, Secretary Michael O. Leavitt announced prevention as one of his top ten priority areas. The overarching agenda of the prevention priority is organized around the four major principles of the HealthierUS initiative:

- Eat a nutritious diet
- Be physically active
- Get your medical screenings
- Make healthy choices

On October 27, 2006, Secretary Leavitt announced plans for the development of federal *Physical Activity Guidelines for Americans* to be issued in 2008 (http://www.hhs.gov/news/press/2006pres/20061026.html). HHS is taking the opportunity to develop the first Physical Activity Guidelines for the nation to serve as the benchmark and single, authoritative voice for providing science-based guidance on physical activity for health promotion. These new, comprehensive guidelines will help promote a culture of wellness in the United States by providing essential and practical information to Americans on physical activity and related health benefits.

To help establish the scientific rationale for physical activity guidelines, HHS sponsored a workshop (October 23 – 24, 2006), organized by the Institute of Medicine, in which a panel of 30 scientists and practitioners reviewed the evidence relating habitual physical activity to various health outcomes, with special emphasis on the prevention of major chronic diseases (http://www.nap.edu/catalog.php?record_id=11819). This overview of existing evidence indicated that frequent participation in physical activity was strongly linked to better health status throughout the life span. Given the high prevalence of sedentary behavior among Americans and the current epidemic of obesity and related diseases, the panel also concluded that federal physical activity guidelines were warranted.

The Physical Activity Guidelines Advisory Committee

Following the announcement by the Secretary, nominations for potential members of a Physical Activity Guidelines Advisory Committee (PAGAC) were sought through a *Federal Register* Notice published in January 2007 (http://a257.g.akamaitech.net/7/257/2422/01jan20071800/edocket.access.gpo.gov/2007/pdf/E7-842.pdf). Prospective members of the Committee were expected to have knowledge of current scientific research in human physical activity and be respected and published experts in their fields; be familiar with the purpose, communication, and application of federal guidelines; and have demonstrated interest in the public's health and well-being through their research and educational endeavors. Expertise was sought in specialty areas related to physical activity, including health promotion and chronic disease prevention; bone, joint, and muscle health and performance; obesity and weight management; musculoskeletal injury and other adverse events; and applications to specific populations such as children, youth, and women during pregnancy and the postpartum period, older adults, persons with disabilities, and diverse races and ethnicities.

To the extent practicable, selection of committee members represented geographic distribution and took into account the needs of the diverse groups served by HHS. Appointments were made without discrimination on the basis of age; race and ethnicity; sex; sexual orientation; disability; or cultural, religious, or socioeconomic status. In February 2007, Secretary Leavitt appointed 13 members to the PAGAC, including a chair and vice chair. The Committee served without pay and worked under the regulations of the Federal Advisory Committee Act.

Charge to the Committee

Secretary Leavitt's charge to the Committee was to "review existing scientific literature to identify where there is sufficient evidence to develop a comprehensive set of specific physical activity recommendations. The Committee is to prepare a report to the Secretary that documents scientific background and rationale for the 2008 edition of the *Physical Activity Guidelines for Americans.* The report will also identify areas where further scientific research is needed. The intent is to have physical activity recommendations for all Americans that will be tailored as necessary for specific subgroups of the population" (http://a257.g.akamaitech.net/7/257/2422/01jan20071800/edocket.access.gpo.gov/2007/pdf/E7-842.pdf).

Committee Meetings

The committee held three 2-day meetings in Washington, DC, that were open to the public and announced in the *Federal Register.* The meetings took place on June 26-27, 2007;

December 6-7, 2007; and February 28-29, 2008. Meeting summaries are available at http://www.health.gov/paguidelines.

Oral comments from the public were presented at the second and third public meetings, and written comments were accepted throughout the tenure of the PAGAC. Written comments were shared with the Committee before the second and third meetings and as Committee members were drafting their final report. These comments are available for examination at the Office of Disease Prevention and Health Promotion, 1101 Wootton Parkway, Suite LL-100, Rockville, MD 20852.

Committee Organization and Work Process

Soon after the PAGAC was convened, members decided that the work of reviewing the science would be best achieved by establishing subcommittees, each of which would review and interpret the literature for specific health outcomes and summarize their findings as a chapter in the report. The subcommittees, composed of Committee members and consultants, communicated by electronic mail and conference calls and held face-to-face meetings before the public Committee meetings. Each subcommittee was responsible for presenting to the full Committee the basis for its conclusions, responding to questions, and making changes if indicated. The conclusions in this report represent the consensus of the entire PAGAC.

Initially, the PAGAC formed 9 subcommittees, focused on the 9 health outcomes identified by the CDC (see below): all-cause mortality, cardiorespiratory health, metabolic health, energy balance, musculoskeletal health, functional health, cancer, mental health, and adverse events. At their first public meeting, members added two other subcommittees: youth and understudied populations (i.e., populations not covered in other chapters — persons with disabilities, women during pregnancy and the postpartum period, and races and ethnicities other than non-Hispanic white).

Each Committee member volunteered to chair one subcommittee and be a member of one or more other subcommittees. To assist in the review process, subcommittee chairs were authorized to select consultants who had scientific expertise in a specific area of the subcommittee's charge (consultants are listed at the beginning of the report).

A Systematic Review of the Evidence on Physical Activity and Health

Immediately after Secretary Leavitt announced plans for the development of federal physical activity guidelines, staff of the Division of Nutrition, Physical Activity, and Obesity (DNPAO) at the Centers for Disease Control and Prevention's (CDC's) National Center for Chronic Disease Prevention and Health Promotion were assigned to develop a process to support the systematic review of the scientific literature relating physical activity to health. The staff developed a conceptual framework for the literature search and a process to systematically abstract published articles and make these abstracts readily accessible to PAGAC members and consultants. The details of this search strategy and process are provided in ***Part F: Scientific Literature Search Methodology***. The product resulting from this search and abstracting process is the *Physical Activity Guidelines for Americans* Scientific Database. CDC staff initially decided to abstract relevant articles published between January 1, 1995 and December 30, 2006. In June 2007, the PAGAC and CDC agreed to expand the abstracting process to include articles published between January 1 and August 10, 2007.

The Committee's Review of the Scientific Literature

PAGAC members were instructed on and encouraged to use the *Physical Activity Guidelines for Americans* Scientific Database to identify articles that would be included in each subcommittee's systematic review of the literature. Also, as each subcommittee developed a plan to review and interpret the scientific data, it made arrangements with the CDC staff and PAGAC leadership for additional abstracting of articles that were central to their review. Because of limited time and resources available, additional abstracting was prioritized based on the importance and relevance of the outcome being addressed. Because not all the relevant literature could be abstracted by the CDC, subcommittees also were encouraged to consider using recent meta-analyses or systematic reviews for various biomarkers or risk factors that appear to be in the causal pathway between activity and a specific clinical outcome (e.g., hypertension or atherogenic lipoproteins for coronary heart disease). Subcommittees were instructed to carefully document in their chapters the literature search and review methods they used.

Following their literature review, each subcommittee drafted a chapter that summarized and synthesized the results of the review. These chapters were subsequently reviewed by at least 3 PAGAC members who were not members of the drafting subcommittee as well as selected consultants. All PAGAC members were encouraged to review all chapters.

Summarizing and Integrating the Science

In addition to summarizing the evidence relating physical activity to individual health outcomes, one of the PAGAC's major goals was to integrate the scientific information on the relation of physical activity and health and to summarize it in a manner that could be used effectively by HHS personnel to develop the Physical Activity Guidelines and related statements.

For the final PAGAC meeting, each subcommittee chair was requested to prepare a brief summary of key findings from their chapter for discussion by PAGAC. Each subcommittee's summary report included information on the type and magnitude of evidence, the strength of the evidence, characteristics of the physical activity most likely to produce the outcome, any evidence of a dose-response association, and any evidence that being sedentary puts a person at increased risk. Selected PAGAC members then were asked to integrate the main conclusions from these subcommittee reports under the headings of youth, adults, older adults, understudied populations, and adverse events. These summary conclusions were presented and discussed at the PAGAC meeting on February 29, 2008. The resulting summary of evidence and consensus statements about the relation of physical activity to health are provided in ***Part E: Integration and Summary of the Science***.

Contents and Organization of the Physical Activity Guidelines Advisory Committee Report

The report includes 3 major components. The first component provides essential background and synthesis information:

- ***Part A: Report Summary*** provides an executive summary of the entire report.
- ***Part B: Introduction*** provides a brief background on the formation of the Physical Activity Guidelines Advisory Committee and the development of their report.
- ***Part C: Key Terms*** defines many of the major terms used throughout the report, including those relating to physical activity, exercise, fitness, health, and measurement.
- ***Part D: Background*** provides context to the current guidelines development effort by briefly describing recent physical activity trends among Americans, by discussing some underlying concepts about physical activity dose response, by briefly describing recent physical activity trends among Americans, and by describing the development of previous physical activity recommendations in the United States.
- ***Part E: Integration and Summary of the Science*** synthesizes the Committee's findings about the relation of physical activity to a broad array of health outcomes.
- ***Part F: Scientific Literature Search Methodology*** explains the development and use of the *Physical Activity Guidelines for Americans* Scientific Database.

The second component, ***Part G: The Science Base,*** includes 11 sections that review and summarize the scientific literature relating physical activity to individual health-related outcomes and populations: all-cause mortality, cardiorespiratory health, metabolic health, energy balance, musculoskeletal health, functional health, cancer, mental health, adverse events, youth, and understudied populations.

The third component, ***Part H: Research Recommendations*** provides a summary of the PAGAC's collective recommendations about key areas of research that should be conducted to further enhance the science base on physical activity and health.

Part C:
Key Terms

This section provides definitions for many of the major terms used in this report and in the scientific literature reviewed during the preparation of the report. We have attempted to use definitions that have been generally accepted in the scientific literature and in major reports and recommendations for physical activity and public health. As scientists, educators, and practitioners continue to strive to better understand new concepts and explore the numerous characteristics of physical activity and their relations to various aspects of health and physical fitness, new terminology is introduced and existing definitions are modified. As new measurement tools are developed and new health outcomes are identified, accepted terminology will continue to evolve as part of the science of physical activity and health.

Included in this section are a number of the terms that pertain to physical activity, physical fitness, and study design. Definitions for disease or condition-specific terms are defined within individual chapters in ***Part G: The Science Base.*** Additional discussion of the terminology used in the presentation of research results or the development of physical activity and public health guidelines can be found in the following publications: *Public Health Aspects of Physical Activity and Exercise* (1), *Toward Active Living* (2), *Physical Activity and Health: A Report of the Surgeon General* (3), *Dose-Response Issues Concerning Physical Activity and Health: An Evidence-Based Symposium* (4), *American College of Sports Medicine's Guidelines for Exercise Testing and Prescription* (5), and *Advancing Physical Activity and Guidelines in Canada* (6).

Physical Activity and Exercise

Two terms are widely used to describe human movement: *physical activity* and *exercise.* Although they are often used interchangeably, their definitions differ.

Physical activity is any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level. Among the ways physical activity can be categorized is according to mode, intensity, and purpose (3). Mode and intensity are defined below. With regard to classification by "purpose," physical activity frequently is categorized by the context in which it is performed. Commonly used categories include occupational, leisure-time or recreational, household, self-care, and transportation or commuting activities. In some studies, sports participation or "exercise training" is assessed and analyzed separately from other leisure-time activities.

Exercise is a subcategory of physical activity that is "planned, structured, and repetitive and purposive in the sense that the improvement or maintenance of one or more components of physical fitness is the objective" (7). *Exercise* and *exercise training* frequently are used interchangeably and generally refer to physical activity performed during leisure time with the primary purpose of improving or maintaining physical fitness, physical performance, or health.

Other terms that describe additional types of physical activity or exercise are defined here:

Activities of daily living. Activities required for everyday living, including eating, bathing, toileting, dressing, getting into or out of a bed or chair, and basic mobility.

Aerobic exercise (training). Exercise that primarily uses the aerobic energy-producing systems, can improve the capacity and efficiency of these systems, and is effective for improving cardiorespiratory endurance.

Anaerobic exercise (training). Exercise that uses the anaerobic energy-producing systems and can improve the capacity of these systems and increase the tolerance of acid-base imbalance during high-intensity exercise.

Balance training. Static and dynamic exercises that are designed to improve individuals' ability to withstand challenges from postural sway or destabilizing stimulus caused by self-motion, the environment, or other objects.

Endurance exercise (endurance training). Exercises that are repetitive and produce dynamic contractions of large muscle groups for an extended period of time (e.g., walking, running, cycling, swimming).

Flexibility exercise. Exercises that enhance the ability of a joint to move through its full range of motion.

Instrumental activities of daily living. Activities related to independent living, including preparing meals, managing money, shopping for groceries or personal items, performing housework, and using a telephone.

Leisure-time physical activity. Physical activities performed by a person that are not required as essential activities of daily living and are performed at the discretion of the person. These activities include sports participation, exercise conditioning or training, and recreational activities such as going for a walk, dancing, and gardening.

Lifestyle activities. This term is frequently used to encompass activities that one carries out in the course of one's daily life, that can contribute to sizeable energy expenditure, e.g., taking the stairs instead of using the elevator, walking to do errands instead of driving, getting off one bus stop earlier, or parking further away than usual to walk to a destination.

Resistance training (strength training, muscle-strengthening activities, or muscular strength and endurance exercises). Exercise training primarily designed to increase skeletal muscle strength, power, endurance, and mass.

Terms related to patterns of physical activity or exercise are defined here:

Accumulation. The concept of meeting a specific physical activity dose or goal by performing activity in short bouts, then adding together the time spent during each of these bouts. For example, a 30-minute per day goal could be met by performing 3 bouts of 10 minutes each throughout the day.

Dose. In the field of physical activity, dose refers to the amount of physical activity performed by the subject or participants. The total dose or amount is determined by the three components of activity: frequency, duration, and intensity. Frequency is commonly recorded as sessions, episodes, or bouts per day or per week. Duration is the length of time for each bout of any specific activity. Intensity is the rate of energy expenditure necessary to perform the activity to accomplish the desired function (aerobic activity) or the magnitude of the force exerted during resistance exercise.

Dose response. The relation between the dose of physical activity and the health or fitness outcome of interest is considered the dose response. The dose can be measured in terms of a single component of activity (e.g., frequency, duration, intensity) or as the total amount. This concept is similar to the prescription of a medication where the expected response will vary as the dose of the medication is changed. The dose-response relation can be linear, exponential, or hyperbolic, and the dose-response relation is likely to vary depending on the primary measure of interest. For example, improvements in cardiorespiratory fitness, bone health, or adiposity are common dose-response measures of interest. A dose of physical activity may exist below which no effect has been detected as well as a dose above which no effect has been detected. These seemingly lowest and highest doses of activity may be called "thresholds," but the term should be used cautiously as these apparent limits may be more related to limitations of measurement than to true biological limits.

Duration. The length of time in which an activity or exercise is performed. Duration is generally expressed in minutes.

Frequency. The number of times an exercise or activity is performed. Frequency is generally expressed in sessions, episodes, or bouts per week.

Intensity. Intensity refers to how much work is being performed or the magnitude of the effort required to perform an activity or exercise. Intensity can be expressed either in *absolute* or *relative* terms.

- ***Absolute.*** The absolute intensity of an activity is determined by the rate of work being performed and does not take into account the physiologic capacity of the individual. For aerobic activity, absolute intensity typically is expressed as the rate of energy expenditure (e.g., milliliters per kilograms per minute of oxygen being consumed, kilocalories per minute, METs) or, for some activities, simply as the speed of the activity (e.g., walking at 3 miles per hour, jogging at 6 miles per hour), or physiologic response to the intensity (e.g., heart rate). For resistance activity or exercise intensity frequently is expressed as the amount of weight lifted or moved.

- ***Relative.*** Relative intensity takes into account or adjusts for a person's exercise capacity. For aerobic exercise, relative intensity is expressed as a percent of a person's aerobic capacity (VO_{2max}) or VO_2 reserve, or as a percent of a person's measured or estimated maximum heart rate (heart rate reserve). It also can be expressed as an index of how hard the person feels he or she is exercising. A person's subjective assessment of how hard he or she is working relative to his/her own capacity is called *rating of perceived exertion*. The Borg Scale is a commonly used numerical scale for rating perceived exertion (8). Rating of perceived exertion is used for both aerobic and muscle-strengthening types of activities.

MET. MET refers to *metabolic equivalent* and 1 MET is the rate of energy expenditure while sitting at rest. It is taken by convention to be an oxygen uptake of 3.5 milliliters per kilogram of body weight per minute. Physical activities frequently are classified by their intensity, using the MET as a reference (see Table D.3 in ***Part D: Background)***.

Mode. The type of activity or exercise that is being performed. Biking, walking, rowing, and weight lifting are all examples of different modes of activity.

Progression. The process of increasing the intensity, duration, frequency, or amount of activity or exercise as the body adapts to a given activity pattern.

Physical Fitness

During the 20th century, **physical fitness** has been defined in a variety of ways, but a generally accepted definition is "the ability to carry out daily tasks with vigor and alertness, without undue fatigue and with ample energy to enjoy leisure-time pursuits and meet unforeseen emergencies" (3, p.20). It has been defined by the World Health Organization as "the ability to perform muscular work satisfactorily" (9, p.6). Physical fitness includes a number of components consisting of cardiorespiratory endurance (aerobic power), skeletal muscle endurance, skeletal muscle strength, skeletal muscle power, flexibility, balance, speed of movement, reaction time, and body composition. Because these attributes differ in their importance to athletic performance versus health, a distinction has been made between *performance-related fitness* and *health-related fitness* (7). Performance-related fitness includes those attributes that significantly contribute to athletic performance and places emphasis on aerobic endurance or power, muscle strength and power, speed of movement, and reaction time. Health-related fitness includes cardiorespiratory fitness, muscular strength and endurance, body composition, flexibility, and balance. The relative importance of any one attribute depends on the specific performance or health goal.

The following terms relate to specific aspects of physical fitness.

Adaptation. The body's response to exercise or activity. Some of the body's structures and functions favorably adjust to the increase in demands placed on them whenever physical activity of a greater amount or higher intensity is performed than what is usual for the individual. It is these adaptations that are the basis for much of the improved health and fitness associated with increases in physical activity.

Agility. A performance-related component of physical fitness that is the ability to change position of the entire body in space with speed and accuracy.

Balance. A performance-related component of physical fitness that involves the maintenance of the body's equilibrium while stationary or moving.

Body composition. A health-related component of physical fitness that applies to body weight and the relative amounts of muscle, fat, bone, and other vital tissues of the body. Most often, the components are limited to fat and lean body mass (or fat-free mass).

Cardiorespiratory fitness (endurance). A health-related component of physical fitness that is the ability of the circulatory and respiratory systems to supply oxygen during sustained physical activity. Usually expressed as measured or estimated maximal oxygen uptake (VO_{2max}).

Coordination. A performance-related component of physical fitness that is the ability to use the senses, such as sight and hearing together with body parts in carrying out motor tasks smoothly and accurately.

Flexibility. A health and performance-related component of physical fitness that is the range of motion possible at a joint. Flexibility is specific to each joint and depends on a number of specific variables, including but not limited to the tightness of specific ligaments and tendons.

Maximal oxygen uptake (VO_{2max}). The body's capacity to transport and use oxygen during a maximal exertion involving dynamic contraction of large muscle groups, such as during running or cycling. It is also known as maximal aerobic power and cardiorespiratory endurance capacity. Peak oxygen consumption (VO_{2peak}) is the highest rate of oxygen consumption observed during an exhaustive exercise test.

Power. A performance-related component of physical fitness that describes the rate (or speed) at which work can be applied.

Speed. A performance-related component of physical fitness that is the ability to perform movements rapidly or within a short period of time.

Strength. A health and performance-component of physical fitness that is the ability of a muscle or muscle group to exert force.

Health

Numerous definitions of **health** exist and, in this report, we have adopted the following: "Health is a human condition with physical, social and psychological dimensions, each characterized on a continuum with positive and negative poles. Positive health is associated with a capacity to enjoy life and to withstand challenges; it is not merely the absence of disease. Negative health is associated with morbidity, and in the extreme, with premature mortality" (10, p.100).

Health-related quality of life is an individual's overall sense of well being and includes such factors as pain, mood, energy level, family and social interactions, sexual function, ability to work, and ability to keep up with routine daily activities.

Study Design and Measurement

Absolute risk. The percentage of subjects in a group that experiences a discrete negative outcome, such as death or hospital admission.

Case-control study. A type of epidemiologic study design in which subjects are selected based on the presence or absence of a specific outcome of interest, such as cancer or diabetes. The individual's past physical activity practices are assessed, and the association between past physical activity and presence of the outcome is determined.

Case report. This includes single case reports of individual patients and published case series.

Confidence interval. When relative risk (see definition below) is calculated, one can also calculate a confidence interval, or a band of uncertainty, around the estimate of the relative risk. Typically, 95% confidence intervals are used in epidemiologic studies. For example, if the estimated relative risk for colon cancer associated with physical activity, compared with inactivity, is 0.5 with a 95% confidence interval of 0.3 to 0.8, this means that we are 95% certain that the true estimate of the relative risk lies between 0.3 and 0.8.

Cross-sectional study. Studies that compare and evaluate specific groups or populations at a single point in time.

Observational studies. Studies in which outcomes are measured but no attempt is made to change the outcome. The two most commonly used designs for observational studies are case-control studies and prospective cohort studies.

Odds ratio. A measure of probability used in epidemiologic studies. It measures the chances of an event (or disease) occurring in one group of people as compared to another group with different characteristics. For example, an odds ratio of 0.5 for high blood pressure in people who participate in physical activity, compared with people who are inactive, indicates that active persons are 0.5 times (50%) less likely to have high blood pressure, compared with those who are inactive (see also **Confidence interval**).

Prospective cohort study. A type of epidemiologic study in which the physical activity practices of the enrolled subjects are determined and the subjects are followed (or observed) for the development of selected outcomes. It differs from clinical trials in that the exposure, in this case physical activity, is not assigned by the researchers.

Randomized controlled trial (also known as a randomized clinical trial). A type of study design in which participants are grouped on the basis of an investigator-assigned exposure of interest, such as physical activity. For example, among a group of eligible participants, investigators may randomly assign them to exercise at three levels: no activity, moderate activity, and vigorous activity. These participants are then followed over time to assess the outcome of interest, such as change in abdominal fat. Randomized controlled trials are often considered the “gold standard” of human intervention study designs. However, because of the cost and issues regarding compliance with an assigned activity level, it may not always be feasible, or even desirable, to conduct this type of trial.

Relative risk. A measure of association used in epidemiologic studies. It measures the magnitude of association between the exposure (such as physical activity) and the disease (such as colon cancer). A relative risk of 0.5 for colon cancer associated with physical activity, compared with inactivity, indicates that active persons have 0.5 times (or 50%) the risk of developing colon cancer compared to inactive persons.

Retrospective study. A study in which the outcomes have occurred before the study has begun.

Publication Types

Cochrane Collaboration. An internationally organized effort to bring existing clinical studies into systematic reviews to facilitate the process of bringing clinical evidence to bear on decisionmaking in patient care.

Meta-analysis. A review of a focused question that follows rigorous methodological criteria and uses statistical techniques to combine data from studies on that question.

Systematic review. A review of a clearly defined question that uses systematic and explicit methods to identify, select, and critically evaluate relevant research, and to collect and analyze data from the studies to include in the review.

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Part D: Background

Introduction

Over the past 35 years, various health associations and agencies in the United States have published guidelines or recommendations for health professionals and the public regarding the health benefits and risks of being physically active. The rationale for these publications was that on the one hand, many people were insufficiently active and needed guidance on why and how to become more physically active, but on the other hand, an increase in physical activity by inactive adults posed significant health risks so medical guidance was needed. To determine how well various segments of the population are meeting these guidelines, national public health surveillance systems have been implemented by agencies within the US Department of Health and Human Services (HHS). The data collected by these surveillance systems over the past decade have indicated that many youth, adults, and older adults fail to meet these recommendations and that the rate of compliance varies substantially by sex, age, educational achievement, socioeconomic status, and race/ethnicity. These results are a major reason for an increased emphasis on developing federal physical activity and public health guidelines and policy statements. In addition, a majority of the questions now being asked about physical activity and health relate more to the dose (type, amount, and intensity) of activity that conveys health benefits in specific populations than to whether or not there are benefits from being physically active. Thus, it is important for the review of the science and the development of physical activity guidelines to carefully consider issues of dose response. This Background addresses all of these issues by discussing several key issues related to dose response, presenting an overview of the recent trends in physical activity by Americans, and outlining the history of physical activity and health recommendations and guidelines in the United States.

Some Issues Regarding Dose Response

Developing physical activity recommendations for public health would be quite easy if simply stated answers could be given to such questions as, “How much activity do I need to be healthy?” or “How much more benefit do I get if I walk 30 minutes 6 times per week verses just 3 times per week?” Unfortunately that does not appear to be the case. To provide an appropriate answer to such questions, a number of issues need to be considered, including a person’s current physical activity status, fitness level, health status, age, sex, and major health and fitness goals. Genetic differences among individuals also influence their responsiveness to a specific dose of activity. All of these issues affect any improvements in health and fitness that may come from increases in various combinations of type, intensity, duration, and frequency (the main components of dose).

The Process of Adaptation

Some of the body's structures and functions favorably adapt to the increase in demands placed on them whenever physical activity of a greater amount or higher intensity is performed than what is usual for the individual. It is these adaptations that are the basis for much of the improved health and fitness associated with increases in physical activity. This increase in activity is called *overload* and if applied correctly, will improve the capacity and/or efficiency of various tissues and systems. For example, cardiac stroke volume and skeletal muscle capillary density are enhanced in response to an increase in aerobic or endurance activity. Many different combinations of the main components of dose can achieve this overload. However, too big an overload applied too quickly can cause fatigue and contribute to injury. Therefore, the overload needs to be applied progressively in relatively small increments to allow for the body to adapt before receiving an even greater overload. This concept is called *progression.* The nature of the adaptation, also called *specificity*, that occurs in response to a progressive overload is influenced by the type of activity being performed. If the overload is produced by aerobic activities like walking, jogging, cycling or swimming, adaptations occur more to the oxygen transport system and various metabolic processes than if the activity is a resistance activity, such as weight lifting, which produces greater changes in muscle strength and mass. Understanding these three principles of the biological responses to activity – overload, progression, and specificity – helps in addressing issues about dose response to activity.

The Baseline Level of Physical Activity

The baseline level of habitual physical activity as well as the exercise capacity (physical fitness) of a person needs to be accounted for when considering an increase in physical activity. In other words, it is important to create an overload but not an excessive amount of overload. Therefore, for a person who has been sedentary for some time for whatever reason, the initial dose of activity should be at a relatively low intensity, of limited duration, with the sessions (also called bouts) spread throughout the week. An example of this approach would be a walking program with sessions of 5 minutes of slow walking, 5 to 6 days per week, with the bouts performed at various times throughout the day (e.g., 3 times per day). As the person adapts to this amount of activity, the bout duration could be slowly increased to 10 minutes, and as exercise capacity begins to increase, the walking speed could be increased. Such an approach is based primarily on expert opinion and clinical experience, as the benefits and risks of various approaches to initiating and progressing an activity program for very sedentary or unfit persons have not been systematically evaluated.

Another issue regarding baseline levels of physical activity is the apparent gradual decline in the recent decade in "routine physical activity" for an increasing proportion of the US population. Unfortunately, in the United States and other developed or developing countries, accurate data are not available on time trends for the total amount of physical activity performed throughout the day (energy expenditure for activities of daily living). Recent reports from objective measures of physical activity using accelerometers for 7 days provide some cross-sectional data on the US population. The results show that a far higher proportion of the population is inactive than has been indicated from self-reported estimates of physical activity (1;2). Very similar data have been reported for adults in Sweden using similar technology (3). We still need to better understand how the results of physical activity assessment by new objective measurement methods that can be applied to large populations compare to data collected by commonly used questionnaires. If the time spent being *physically inactive* is continuing to increase among the US population, it may be that the starting dose of activity will need to be adjusted downward to accommodate more people with lower exercise capacities. At the same time, the amount of activity that will have to be added to this lower baseline to return people to being physically active by current day standards will have to be increased.

Physical Activity Intensity

Intensity is a key factor when considering the dose of physical activity required to achieve specific health and fitness outcomes. Not only does an increase in activity intensity play a major role in producing many favorable adaptations, but it also has a key role in the risk of injury during activity. In most of the studies reviewed for this report, the intensity of physical activity was expressed either in *absolute* or *relative* values. *Absolute* intensity refers to the energy or work required to perform the activity and does not take into account the physiologic capacity of the individual. For aerobic activity, *absolute* intensity may be expressed as the rate of energy expenditure (e.g., kilocalories per minutes, multiples of resting energy expenditure [METs]) or, for some activities, simply as the speed of the activity (e.g., walking at 3 miles per hour, jogging at 6 miles per hour). For resistance exercise, absolute intensity is expressed as weight lifted or force exerted (e.g., pounds, kilograms). Absolute intensity also can be classified into categories such as light, moderate, hard, and very hard (Table D.1).

Table D.1. Classification of Physical Activity Intensity

Endurance Type Activity — Relative Intensity

Intensity	Percent VO_2R* Percent HRR	Percent HR_{max}[¥]	RPE[†]
Very Light	<20	<50	<10
Light	20-39	50-63	10-11
Moderate	40-59	64-76	12-13
Hard	60-84	77-93	14-16
Very Hard	≥85	≥94	17-19
Maximal	100	100	20

Table D.1. Classification of Physical Activity Intensity (continued)

Endurance Type Activity — Intensity (METs and %VO_{2max}) in Healthy Adults Differing in VO_{2max}

Intensity	VO_{2max} = 12 METs METs	VO_{2max} = 12 METs Percent VO_{2max}**	VO_{2max} = 10 METs METs	VO_{2max} = 10 METs Percent VO_{2max}	VO_{2max} = 8 METs METs	VO_{2max} = 8 METs Percent VO_{2max}	VO_{2max} = 5 METs METs	VO_{2max} = 5 METs VO_{2max}
Very Light	<3.2	<27	<2.8	<28	<2.4	<30	<1.8	<36
Light	3.2-5.3	27-44	2.8-4.5	28-45	2.4-3.7	30-47	1.8-2.5	36-51
Moderate	5.4-7.5	45-62	4.6-6.3	46-63	3.8-5.1	48-64	2.6-3.3	52-67
Hard	7.6-10.2	63-85	6.4-8.6	64-86	5.2-6.9	65-86	3.4-4.3	68-87
Very Hard	≥10.3	≥86	≥8.7	≥87	≥7.0	≥87	≥4.4	≥88
Maximal	12	100	10	100	8	100	5	100

Resistance-Type Exercise

Intensity	Relative Intensity Percent 1RM§
Very Light	<30
Light	30-49
Moderate	50-69
Hard	70-84
Very Hard	≥85
Maximal	100

*%VO_2R – percent of oxygen uptake reserve; %HRR – percent of heart rate reserve
¥%HR_{max} = 0.7305 (%VO_{2max}) + 29.95 (4); values based on 10-MET group
†Borg Rating of Perceived Exertion 6-20 scale (5)
**%VO_{2max} = [(100%-%VO_2R) MET_{max}^{-1}] + %VO_2R; personal communication (6)
§RM = repetitions maximum, the greatest weight that can be moved once in good form

From: Howley, E. Med Sci Sports Ex. S364-S369, 2001. (7)

Some previous physical activity and health recommendations (8), defined absolute moderate intensity as 3.0 to 6.0 METs and vigorous intensity as more than 6.0 METs. After carefully reviewing these classifications, the PAGAC recommends that moderate intensity be defined at 3.0 to 5.9 METs and vigorous intensity as 6.0 or greater METs. This redefinition means that a number of activities classified as 6.0 METs would now be considered vigorous intensity rather than moderate intensity. A list of activities classified as 6.0 METs in the Compendium of Physical Activity (9) is included in Table D.2.

Table D.2. Physical Activities Listed as 6.0 METs in the Compendium of Physical Activities

Compendium Code (2000)	METs	Heading (Activity Group)	Activity Description
2050	6	Conditioning exercise	Weight lifting (free weight, nautilus or universal-type), power lifting or body building, vigorous effort (Taylor Code 210)
2090	6	Conditioning exercise	Slimnastics, jazzercise
2110	6	Conditioning exercise	Teaching aerobic exercise class
4050	6	Fishing and hunting	Fishing in stream, in waders (Taylor Code 670)
4080	6	Fishing and hunting	Hunting, deer, elk, large game (Taylor Code 170)
4110	6	Fishing and hunting	Hunting, pheasants or grouse (Taylor Code 680)
5120	6	Home activities	Moving furniture, household items, carrying boxes
6050	6	Home repair	Carpentry, outside house, installing rain gutters, building a fence, (Taylor Code 640)
6180	6	Home repair	Roofing
8020	6	Lawn and garden	Chopping wood, splitting logs
8060	6	Lawn and garden	Gardening with heavy power tools, tilling a garden, chain saw
8110	6	Lawn and garden	Mowing lawn, walk, hand mower (Taylor Code 570)
8200	6	Lawn and garden	Shoveling snow, by hand (Taylor Code 610)
11030	6	Occupation	Building road (including hauling debris, driving heavy machinery)
11100	6	Occupation	Coal mining, general
11192	6	Occupation	Farming, taking care of animals (grooming, brushing, shearing sheep, assisting with birthing, medical care, branding)
11320	6	Occupation	Forestry, planting by hand
11380	6	Occupation	Horse grooming
11560	6	Occupation	Shoveling, light (less than 10 pounds/minute)
11780	6	Occupation	Using heavy power tools such as pneumatic tools (jackhammers, drills, etc.)
12010	6	Running	Jog/walk combination (jogging component of less than 10 minutes) (Taylor Code 180)
15050	6	Sports	Basketball, non-game, general (Taylor Code 480)
15110	6	Sports	Boxing, punching bag

Table D.2. Physical Activities Listed as 6.0 METs in the Compendium of Physical Activities (continued)

Compendium Code (2000)	METs	Heading (Activity Group)	Activity Description
15190	6	Sports	Drag racing, pushing or driving a car
15200	6	Sports	Fencing
15500	6	Sports	Paddleball, casual, general (Taylor Code 460)
15640	6	Sports	Softball, pitching
15680	6	Sports	Tennis, doubles (Taylor Code 430)
15730	6	Sports	Wrestling (one match = 5 minutes)
15733	6	Sports	Track and field (high jump, long jump, triple jump, javelin, pole vault)
16040	6	Transportation	Pushing plane in and out of hangar
17027	6	Walking	Carrying 16 to 24 lb load, upstairs
17080	6	Walking	Hiking, cross country (Taylor Code 040)
17210	6	Walking	Walking, 3.5 mph, uphill
18150	6	Water activities	Skiing, water (Taylor Code 220)
18300	6	Water activities	Swimming, lake, ocean, river (Taylor Codes 280, 295)
18310	6	Water activities	Swimming, leisurely, not lap swimming, general
19010	6	Winter activities	Moving ice house (set up/drill holes, etc.)
19160	6	Winter activities	Skiing, downhill, moderate effort, general

NOTE: This table is adapted from *The Compendium of Physical Activities* (9).

In contrast, *relative* intensity takes into account or adjusts for a person's exercise capacity. For aerobic exercise, *relative* intensity is expressed as a percent of a person's aerobic capacity (VO_{2max}) or VO_2 reserve, as a percent of a person's measured or estimated maximum heart rate or heart rate reserve, or as an index of how hard the person feels he or she is exercising (rating of perceived exertion) (10). A percent of maximum heart rate or heart rate reserve can be used because a near linear relation exists between the increase in heart rate and the increase in oxygen uptake during dynamic aerobic exercise. Table D.1 also provides the classification of physical activity intensity showing the relation between absolute and relative intensity for aerobic activity and relative intensity for resistance exercise.

In most experimental studies evaluating the effects of increased activity on various fitness and health outcomes, intensity is expressed relative to each person's capacity (e.g., 60% to 75% of VO_{2max}). However, in nearly all of the large prospective observational studies, physical activity intensity is expressed in absolute terms (no adjustment made for each person's exercise capacity). These differences in methodology limit to some degree direct comparison of dose-response data from these 2 major sources of evidence. For an activity of a given absolute intensity, such as walking at 3.0 miles per hour (3.3 METs), the relative intensity varies inversely to the aerobic capacity of the individual. As shown in Figure D.1, for highly fit people with an aerobic capacity of 14 METs, walking at 3.0 miles per hour has a relative intensity of 24 % (left y-axis) or light intensity (right y-axis), but for people of low fitness who have only a 4-MET capacity, the relative intensity is at 83% (left y-axis) or hard intensity (right y-axis). A similar situation is displayed for a walking speed of 4.0 miles per hour with a MET value of 5.0. Note that it is impossible for people with a 4-MET capacity to walk this fast for an extended period of time, as the energy requirement exceeds their aerobic capacity. Standardization of activity intensity classification is essential for accurately establishing the relation between intensity and health or fitness outcomes.

Figure D.1. The Relative Exercise Intensity for Walking at 3.0 mph (3.3 METs) and 4.0 mph (5.0 METs) Expressed as a Percent of VO_{2max} for Adults With an Exercise Capacity Ranging from 4 to 14 METs

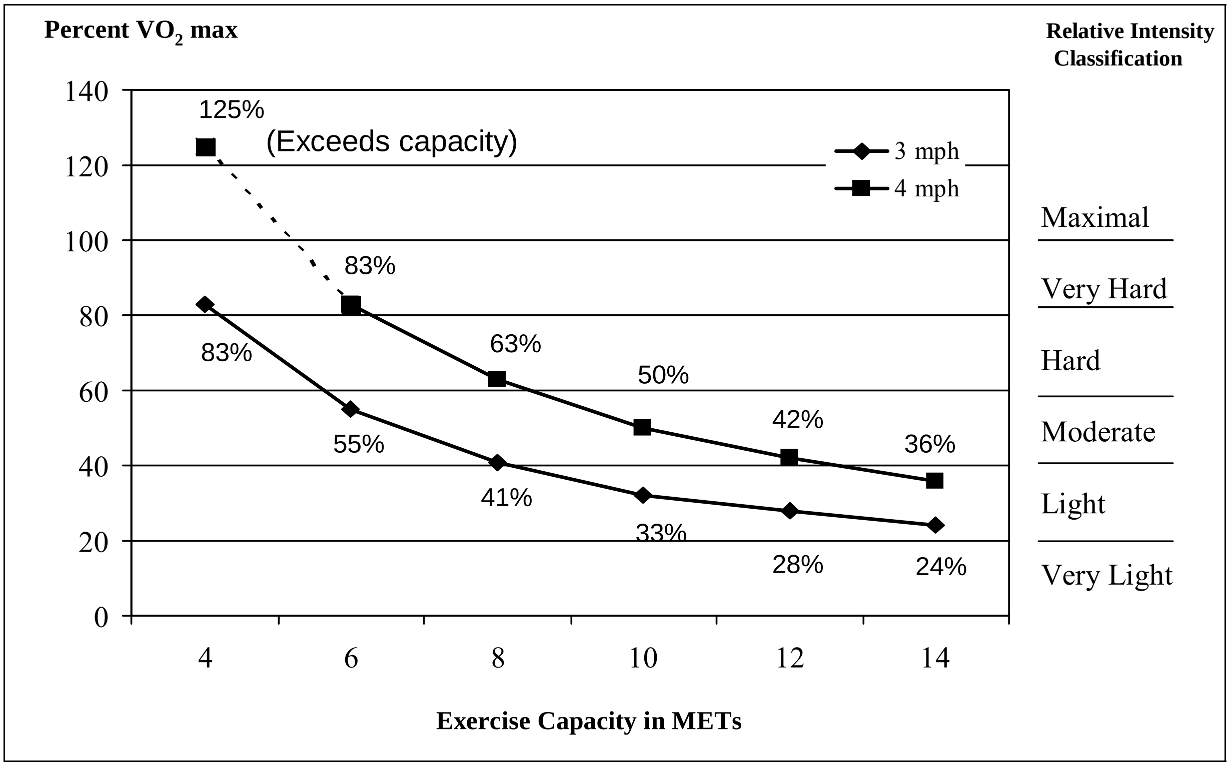


Figure D.1. Data Points

Exercise Capacity	METs 4	METs 6	METs 8	METs 10	METs 12	METs 14
3 mph	83	55	41	32	28	24
4 mph	–	83	63	50	42	36

Physical Activity Amount

The amount of physical activity performed by a person for a given period of time is the product of activity duration, absolute intensity, and frequency. Thus, the amount of activity is one expression of activity dose. For many of the prospective observational studies cited in this review, the primary activity exposure is the amount of leisure-time or total physical activity expressed in minutes or hours per day or week (of moderate, vigorous, or moderate plus vigorous activity), distance walked or jogged/run per day or week. Exposure also can be the estimated amount of energy expended expressed in kilocalories per day or week, kilocalories per kilogram of body weight per day or week, or MET-minutes or MET-hours per day or week.

In experimental studies, the amount of activity sometimes has been expressed in these same units but also has been given with the intensity in relative units along with the frequency and duration of the activity sessions with no overall amount or volume of activity provided (e.g., 30 minutes at 70% heart rate reserve [HRR], 5 times per week for 24 weeks). To pool or compare results across studies and develop generalized conclusions about the benefits provided with various amounts of physical activity, it was necessary to be able to compare one expression of the amount of activity with others. Table D.3 provides this type of information for walking, jogging, and running over a range in activity intensity from 3.0 to 16.0 METs.

Table D.3. Walk, Jog, and Run Speeds and METs, MET-Minutes, MET-Hours, and Distance (miles) for 2.5 Hours (150 min) and 5.0 Hours (300 min) per Week of Physical Activity. Also Listed Are the Estimated Kilocalories (kcal) Expended by a 75 kg (165 lb) Adult During 150 and 300 Minutes per Week at the Different Intensities of Activity.

Speed (mph)	METs	For 2.5 hr/wk (150 min/wk) MET-min	For 2.5 hr/wk (150 min/wk) MET-hours	For 2.5 hr/wk (150 min/wk) Miles	For 2.5 hr/wk (150 min/wk) kcal	For 5.0 hr/wk (150 min/wk) MET-min	For 5.0 hr/wk (150 min/wk) MET-hours	For 5.0 hr/wk (150 min/wk) Miles	For 5.0 hr/wk (150 min/wk) kcal
Rest	1.0	150	2.5	0.0	190	300	5.0	0.0	380
2.5	3.0	450	7.5	6.25	565	900	15.0	12.5	1,130
3.0	3.3	495	8.25	7.5	620	990	16.5	15.0	1,240
4.0	5.0	750	12.5	10.0	940	1,500	25.0	20.0	1,880
4.3	6.0	900	15.0	10.75	1,125	1,800	30.0	21.5	2,250
5.0	8.0	1,200	20.0	12.5	1,500	2,400	40.0	25.0	3,000
6.0	10.0	1,500	25.0	15.0	1,875	3,000	50.0	30.0	3,750
7.0	11.5	1,725	28.25	17.5	2,155	3,450	56.5	35.0	4,310
8.0	13.5	2,025	33.75	20.0	2,530	4,050	67.5	40.0	5,060
10.0	16.0	2,400	40.0	25.0	3,000	4,800	80.0	50.0	6,000

2.5 - 4.3 mph = walk
5-10 mph = jog/run
† kilocalories for 75 kg adult when exercising at the given intensity for either 150 or 300 minutes.

Note: These are gross energy expenditure values during exercise; thus, they include the energy expenditure at rest and not just the additional energy expenditure due to the activity. Kilocalories calculated using 1 MET = 1 kilocalorie per kilogram per hour and rounded to nearest 5 kilocalories. MET values from Ainsworth and colleagues (9).

Based on data in this table, for 2.5 hours per week of activity at moderate absolute intensity (3.0 to less than 6.0 METs), a person would have a range for MET-minutes per week of 450 to less than 900, MET-hours per week of 7.5 to less than 15.0 and, if they weighed 165 pounds (75 kilograms), their kilocalories of energy expenditure would range from 565 to less than 1,125 kilocalories. If this were achieved by walking at various speeds, the distance would range from 6.25 to less than 10.75 miles per week. At 5 hours per week of moderate-intensity activity, the MET-minutes per week would range from 900 to less than 1,800 and MET-hours per week would range from 15.0 to less than 30.0. Kilocalories expended by a 165-pound (75 kilogram) adult would range from 1,130 to less than 2,250 and the distance walked would be 12.5 to less than 21.5 miles.

The energy expenditure values in Table D.3 are estimated gross values. They include both the energy expenditure required at rest (1 MET) as well as the added (net) energy expenditure required for performing the activity. The estimated energy expenditure for a 165-pound (75 kilogram) person at rest for 150 minutes during the week is about 190 kilocalories. If that person instead walked at a 3.0 mile per hour pace for the 150 minutes, his or her estimated energy expenditure during this time would be about 620 kilocalories, or an increase above rest of 430 kilocalories. However, if the person jogged at a 6 mile per hour pace for these 150 minutes, he or she would expend approximately 1,875 kilocalories, or an increase above rest of about 1,685 kilocalories. Thus, a 165-pound person jogging at 6 miles per hour for 150 minutes per week would expend approximately 1,255 more kilocalories than if he or she walked at 3 miles per hour for the same amount of time during the week. This example demonstrates the substantial increase in energy expenditure as the intensity of the activity increases. In this example, the *increase* in kilocalories while jogging is nearly 4 times greater than the increase while walking (430 versus 1,655).

Recent Trends in Physical Activity in the United States

Since the 1995 physical activity and public health recommendations published by the Centers for Disease Control and Prevention and the American College of Sports Medicine (8) and *Physical Activity and Health: A Report of the Surgeon General* published in 1996 (11), national health behavior surveillance systems have collected cross-sectional information on self-reported compliance with these recommendations by representative samples of Americans. The major national public health surveillance systems monitoring physical activity in the US population include the Behavioral Risk Factor Surveillance System (BRFSS; http://www.cdc.gov/brfss/), the Youth Risk Behavior Surveillance System (YRBSS; http://www.cdc.gov/HealthyYouth/yrbs/), National Health and Nutrition Examination Survey (NHANES; http://www.cdc.gov/nchs/nhanes.htm), and the National Health Interview Survey (NHIS; http://www.cdc.gov/nchs/nhis.htm). For details regarding the methodologies used by each of these surveys, readers are referred to their respective websites. These surveys provide snapshots of participation in selected types or categories of activities by adults and youth and participation in structured programs of activity, such as physical education and organized sports in youth. They include measures of inactivity as well as of activity and, in many cases, include information through 2005. No surveillance system exists that captures an overall determination of physical activity performed or the energy expended during activity throughout the day – during work, school, home and self care, commuting, and leisure time. However, one systematic review of physical activity trends over the past 50 years suggest that declines have occurred in work-related activity, self-transportation activity, and activity in the home, resulting in overall decrease in physical activity (12).

Adults and Older Adults

The BRFSS is a state-based random-digit dialed telephone survey of the non-institutionalized US civilian population aged 18 years and older. Beginning in 2001, BRFSS included biannual questions about leisure-time physical activity asking whether respondents participated in either moderate- or vigorous-intensity activity in bouts of at least 10-minute duration. If they did, respondents were asked to report the frequency and duration of these activities (13). Participants who reported at least 30 minutes of moderate-intensity activity 5 or more days per week or 20 minutes of vigorous-intensity activity 3 or more days per week, or both were considered to be engaged in regular physical activity and to meet current recommendations. In 2005, the prevalence of women reporting that they regularly engaged in physical activity was 46.7%, which was a relative increase of 8.6% from 2001 (43.0%), while men increased 3.5%, from 48.0% to 49.7%. For women, a significant increase between 2001and 2005 was reported in all racial/ethnic groups and all age and education level categories except for women aged 18 to 24 years (Figure D.2). Among men, significant increases were observed for the age range 45 to 64 years, non-Hispanic whites, non-Hispanic blacks, high school graduates and college graduates.

As can be seen in Figure D.2, the percentage of men who reported being physically active is greater than for women and steadily declines with age in both sexes. The prevalence at age 18 to 24 years is 60.5% for men and 50.8% for women, but significantly decreases by age 65 years and older to 43.1% in men and 32.2% in women. For both men and women, higher levels of education were associated with a higher prevalence of reporting being physically active, ranging from 35.5% and 34.2% for men and women who had not graduated from high school up to 52.6% and 49.1% for men and women who were college graduates. Non-Hispanic white men and women tend to have a higher reported prevalence of being active than other racial/ethnic groups with the largest differences in 2005 being between non-Hispanic white and black women and between non-Hispanic white men and Hispanic men.

The data presented in Figure D.2 are quite consistent with self-report data from other national surveys conducted over the past decade.

Figure D.2. Estimated Age Adjusted Percentage of Persons ≥18 Years Reported Meeting the Healthy People 2010 Objective for Regular Physical Activity in 2001 and 2005: Data from BRFSS

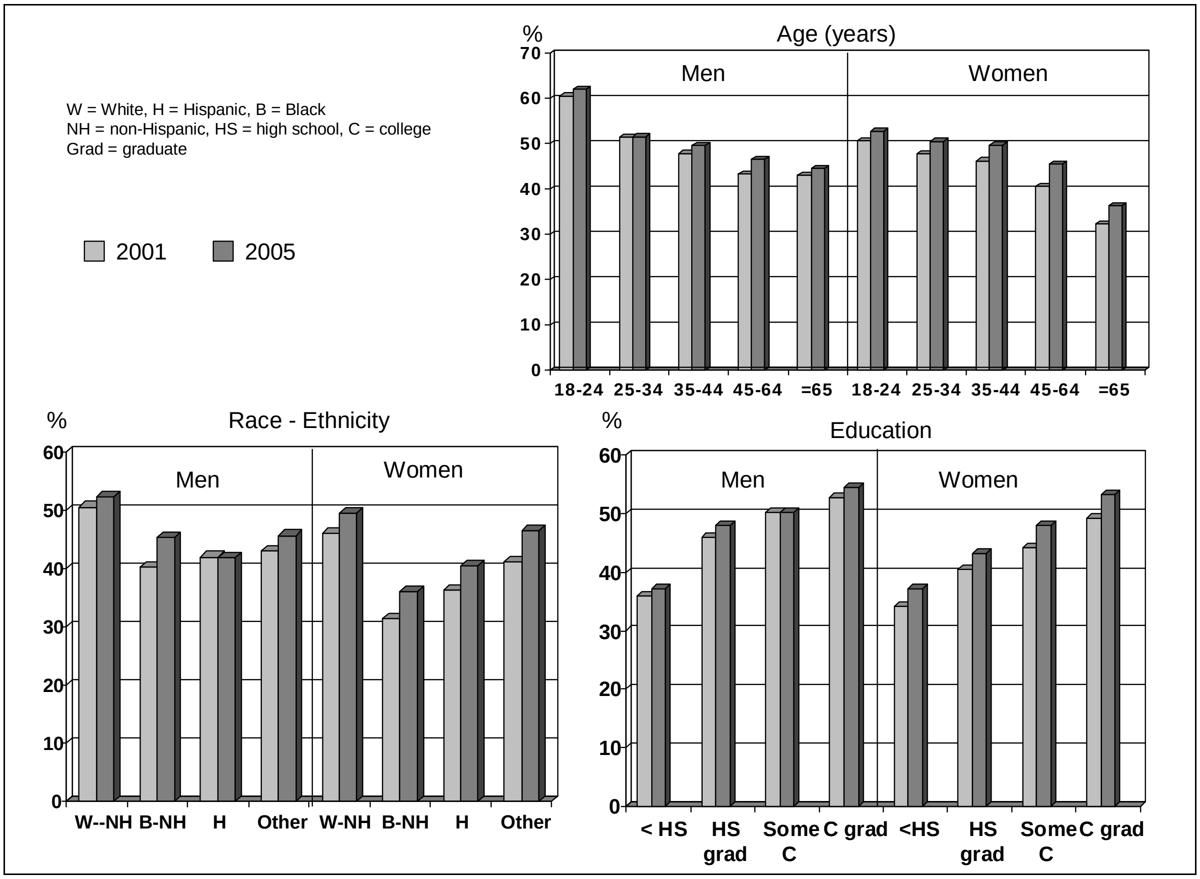


Figure D.2. Data Points Age

Year	Men 18-24	Men 25-34	Men 35-44	Men 45-64	Men *65	Women 18-24	Women 25-34	Women 35-44	Women 45-64	Women *65
2001	60.5	51.4	47.8	43.3	43.1	50.6	47.7	46.2	40.6	32.2
2005	62	51.5	49.6	46.5	44.5	52.7	50.5	49.7	45.5	36.3

Figure D.2. Data Points Race — Ethnicity

Year	Men W--NH	Men B-NH	Men H	Men Other	Women W-NH	Women B-NH	Women H	Women Other
2001	50.6	40.3	42	43.1	46	31.4	36.3	41.2
2005	52.3	45.3	41.9	45.7	49.6	36.1	40.5	46.6

Figure D.2. Data Points Education

Year	Men < HS	Men HS grad	Men Some C	Men C grad	Men <HS	Men HS grad	Men Some C	Men C grad
2001	35.8	46	50.3	52.6	34.2	40.3	44.3	49.1
2005	37.2	47.9	50.3	54.6	37.1	43.2	47.9	53.3

Figure D.3 displays data from the Healthy People 2010 Database (DATA2010) for men and women combined for selected measures of physical activity reported annually from 1997 to 2006 (14). Over this period, 30% to 35% of adults reported participation in moderate- or vigorous-intensity activity sufficient to meet existing recommendations, and those reporting no leisure time activity remained in the 35% to 40% range. Neither of these measures showed a consistent trend over time. From 1997 through 2000, approximately 16% of the adult population reported performing muscle strength and endurance exercises, with an increase to about 20% being reported from 2001 to 2006.

Figure D.3. Reported Physical Activity by Adults in the USA: 1997-2006 The Healthy People 2010 Database

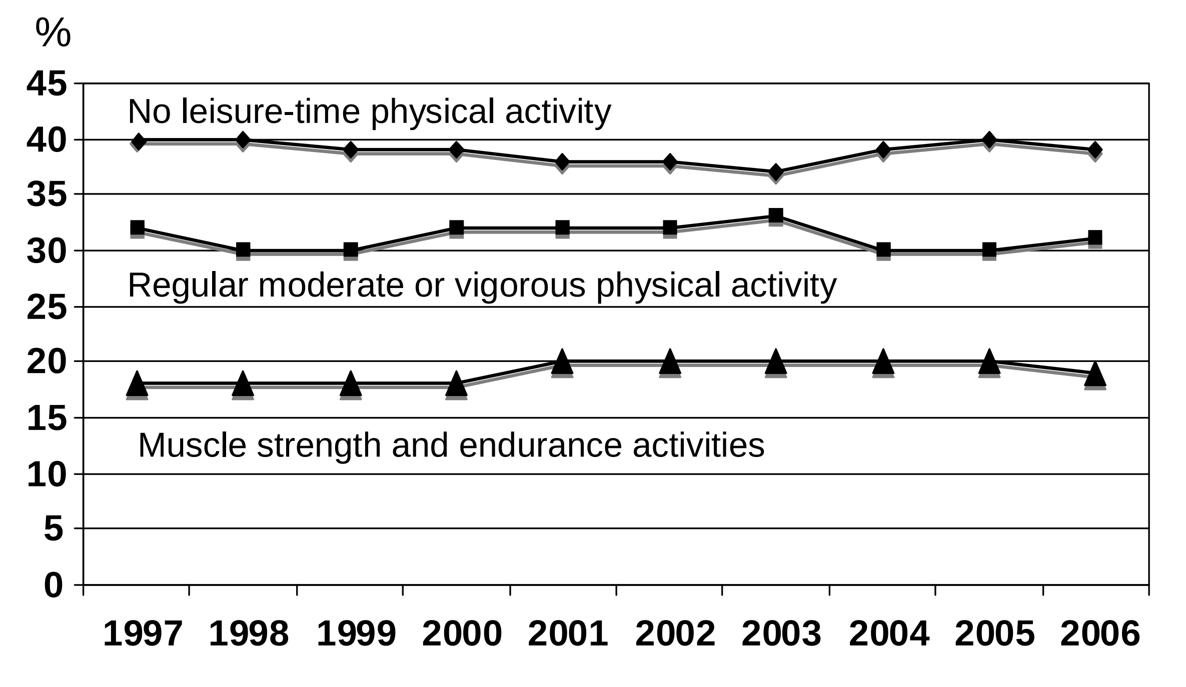
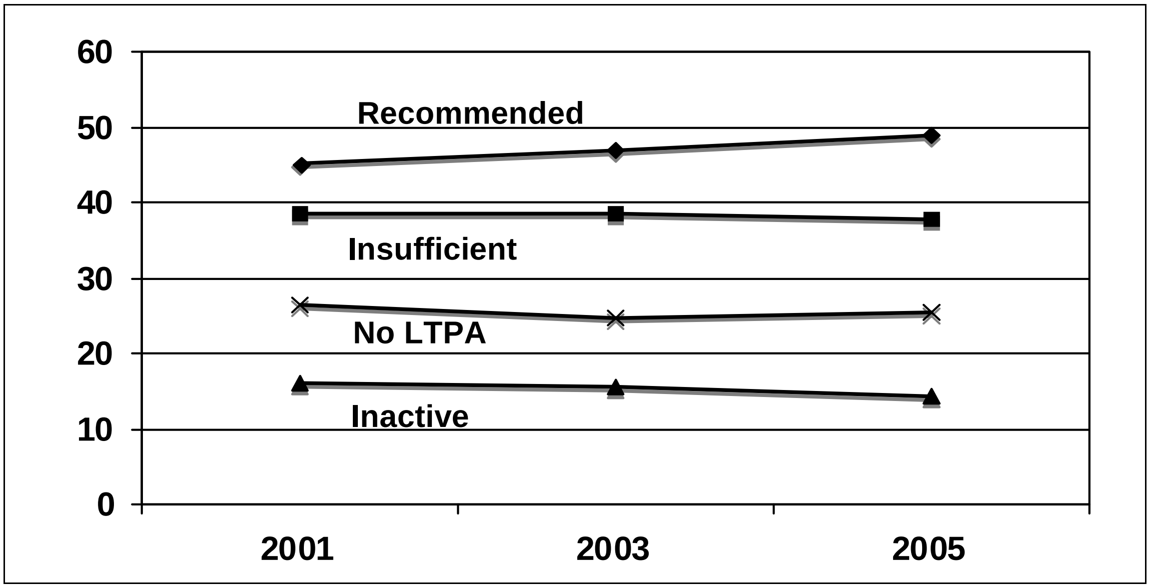


Figure D.3. Data Points

Activity	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
No leisure-time physical activity	40	40	39	39	38	38	37	39	40	39
Regular moderate or vigorous physical activity	32	30	30	32	32	32	33	30	30	31
Strength and endurance activities	18	18	18	18	20	20	20	20	20	19

Depending on how the questions are asked and the activity classification criteria used, responses to the various national physical activity surveillance systems indicate that 45% to 50% of adults in the US report meeting current public health recommendations for moderate-to-vigorous physical activity (defined as moderate-intensity activities [i.e., brisk walking, bicycling, vacuuming, gardening, or anything else that causes small increases in breathing or heart rate] for at least 30 minutes per day at least 5 days per week, or vigorous-intensity activities [i.e., running, aerobics, heavy yard work, or anything else that causes large increases in breathing or heart rate] for at least 20 minutes per day at least 3 days per week, or both). About 38% to 40% report being insufficiently active (defined as doing more than 10 minutes total per week of moderate- or vigorous-intensity lifestyle activities [i.e., household, transportation, or leisure-time activity] but less than the recommended level of activity). Around 25% report performing no moderate-to-vigorous physical activity during leisure time (defined as no physical activities or exercises such as running, calisthenics, golf, gardening, or walking in the previous month), and approximately 15% are considered inactive (defined as less than 10 minutes total per week of moderate- or vigorous-intensity lifestyle activities [i.e., household, transportation, or leisure-time activity]. Figure D.4 provides data from the BRFSS for 2001-2005 for all adults combined (13).

Figure D.4. Reported Physical Activity by Adults in the USA: 2001-2005 Data from BRFSS



"Recommended," "Insufficient," and "Inactive" data comprise one measure, and responses should sum to ~100%. "No Leisure-Time Physical Activity" is a separate question, and should not be included with calculations for the recommended, insufficient, or inactive.

Figure D.4. Data Points

Physical Activity	2001	2003	2005
Recommended	45.3	46.9	48.8
Insufficient	38.6	38.5	37.7
No leisure-time physical activity	26.3	24.6	25.4
Inactive	16.0	15.6	14.2

Youth

Based on data from the YRBSS for 2005, 35.8% of high school students reported meeting current physical activity recommendations (defined as performing any kind of physical activity that increased their heart rate and made them breathe hard some of the time (i.e., moderate or vigorous intensity) for at least 60 minutes per day on 5 or more days of the 7 days preceding the survey) (5). The reported prevalence of meeting this level of physical activity was higher in boys (43.8%) than girls (27.8%) and higher in white (46.9%), black (38.2%), and Hispanic (39.0%) boys than for white (30.2%), black (21.3%), and Hispanic (26.5%) girls. Prevalence estimates of meeting current recommendations of at least 60 minutes per day 5 or more days per week of moderate- or higher-intensity activity ranged from 26.9 to 45.9% across state surveys (median 33.9) for students in grades 9-12.

The recommended level of physical activity used as a benchmark by the YRBSS before the 2005 survey was either 20 minutes of vigorous-intensity activity (activities that make a person sweat and breathe hard) at least 3 days per week or at least 30 minutes of moderate-intensity activity (activity that does not cause a person to sweat or breathe hard) on at least 5 days per week. The percentage of students meeting these recommendations in 2005 was substantially higher than for the updated 60 minutes per day recommendations: boys (75.8%) were higher than girls (61.5 %) and white (77.0%), black (71.7%), and Hispanic (76.0) boys had higher compliance rates than did white (63.3%), black (53.1%), and Hispanic (62.6%) girls. Students reporting not participating in any moderate or vigorous intensity activity during the past 7 days was 7.6% nationwide, with a higher prevalence among girls (11.3%) than among boys (7.9%) and higher among black (14.4%) than white (8.1%) and Hispanic students (10.6%).

In 2005, 54.2% of high school students reported attending a physical education (PE) class one or more days per week on an average week they were in school with a higher percentage of boys (60.0%) reporting yes than girls (48.3%) and higher percentages of white (58.1%), black (61.7%), and Hispanic (65.9%) boys reporting yes than white (46.1%), black (50.5%), and Hispanic (57.5%) girls. The prevalence of attending PE class at least one day per week varied by state from a low of 25.2% to a high of 94.2%. However, when the frequency criteria for attending PE class was increased from 1 day per week to 5 days in an average week, the prevalence decreased to 37.1% for boys and 29.0% for girls, with the variation among states ranging from 6.7% to 60.7%.

Based on data from the various physical activity questions contained in the YRBSS for 2005, high school boys tend to meet moderate-to-vigorous physical activity recommendations more frequently than do girls, with this sex difference being true for white, black, and Hispanic youth. Overall, it appears that white high school students report being somewhat more active than Hispanic and black students, but their attendance in PE classes does not appear to be any different.

Figure D.5 displays the trends for various indices of physical activity for high school students for the period 1999-2005 collected using the YRBSS (14). Included are the percentage of students who met the previous recommendations of either moderate- or vigorous-intensity activity, students reporting no moderate or vigorous physical activity, and the percentage of students reporting attending PE class 5 days per week on average or at least one day per week. The overall impression gained from the data displayed in this figure is that over this 7-year period, neither reported activity meeting moderate-to-vigorous physical activity recommendations or attendance in high school PE classes changed much. The prevalence of students not reporting any moderate-to-vigorous physical activity over the past week also has remained quite constant.

Figure D.5. Percent of High School Students in the United States with Various Physical Activity Profiles: 1999-2005 Data from YBRFSS

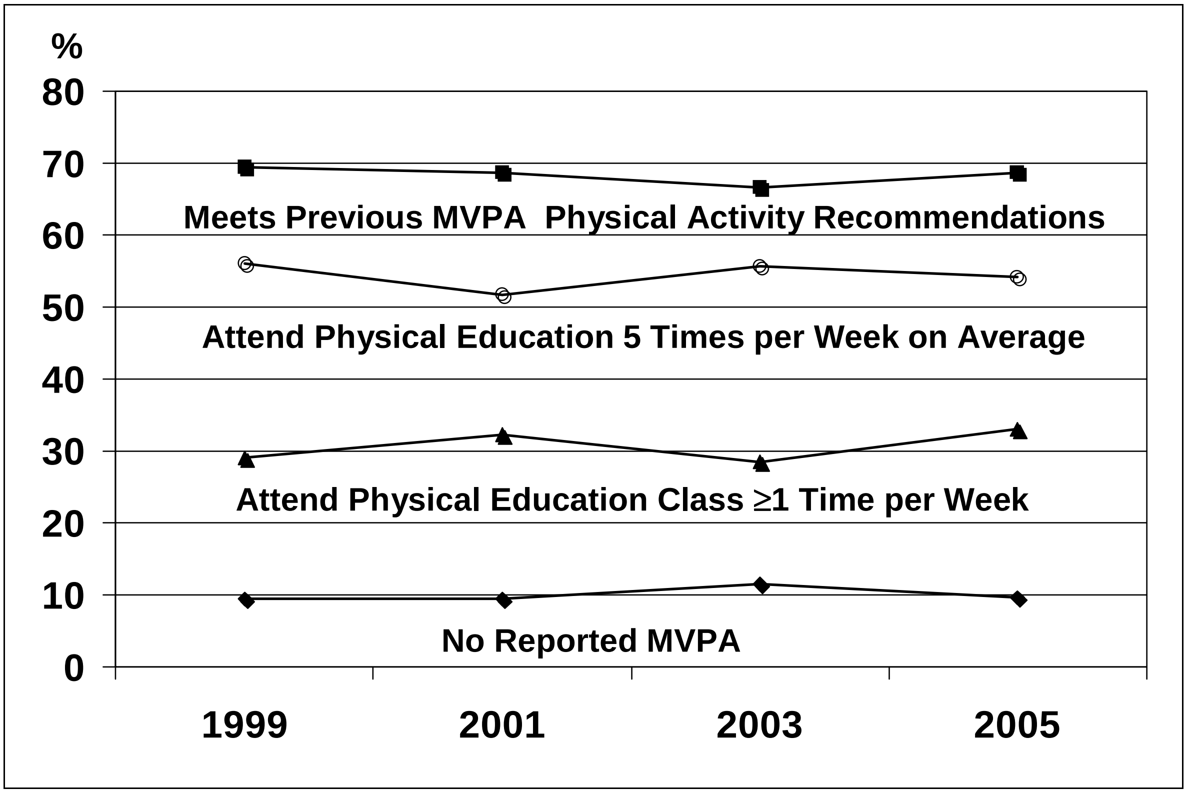


Figure D.5. Data Points

Activity	1999	2001	2003	2005
Meet moderate or vigorous physical activity	69.5	68.6	66.6	68.7
Physical education class 5 times per week	56.1	51.7	55.7	54.2
Physical education class ≥1 time per week	29.1	32.2	28.4	33
No moderate or vigorous physical activity	9.4	9.5	11.5	9.6

Comment on Measures of Physical Activity Trends in the United States

As mentioned previously, no national surveillance system in the United States attempts to document all activity performed throughout the day. Also, no national surveillance system exists to track physical activity of young children not yet in high school or to specifically target the rapidly increasing older population. The results of the national surveillance systems cited above generally indicate some small changes in the activity status of youth and adults in the past 5 to 10 years, primarily based on whether or not they meet current physical activity recommendations. Data from the BRFSS for 2001-2005 do demonstrate a 6% or so relative increase in adults meeting moderate-to-vigorous physical activity recommendations, and other BRFSS data for the period 1994-2004 indicate that the percentage of the population who reported no LTPA decreased from 29.8% in 1994 to 23.7% in 2004 (13). However data collected using the NHIS indicate that the percentage of adults who engaged in regular leisure-time physical activity did not change between 1997 and 2006.

Overall, the data provided by these national surveillance programs consistently demonstrate that a majority of adults do not meet current physical activity and public health recommendations. Although about two-thirds of high school students report meeting previous moderate-to-vigorous physical activity recommendations (at least 30 minutes of moderate intensity activity at least 5 days per week, or vigorous intensity activity at least 20 minutes at least 3 times per week), only 35.8% report meeting the current recommendations (at least 60 minutes per day of moderate or vigorous intensity activity on at least 5 days per week) (5). Also, any changes in the various indices of physical activity for high school students have been small and inconsistent over the past decade.

The use of self-report instruments to monitor physical activity over time is known to have a variety of limitations given the diversity of activities that are performed daily by people with different jobs, home care responsibilities, commuting patterns, and leisure-time pursuits. Attempting to obtain adequate detail so that accurate classifications of activity status can be made based on type, intensity, and amount of activity is difficult and can lead to inaccurate information and increased non-response. Until recently, no real option existed for collecting physical activity surveillance data other than by self-report. However, over the past decade, the technology of objective physical activity monitors, especially accelerometers, that can be used in large and diverse populations has developed substantially. Initially, these monitors were used in small-scale studies, but accelerometer data describing the physical activity patterns in relatively large (n=1,100 to 6,800) samples (1-3) has recently been published. These initial reports demonstrate the substantial potential for the use of such devices in national physical activity surveillance programs but also present a challenge for analyzing the large amounts of data they produce and interpreting results. For example, accelerometers were used to collect NHANES data minute by minute during waking hours over 7 days in approximately 6,800 children, adolescents, and adults (1). Based on these data, 42% of children aged 6 to 11 years met the current 60 minutes per day recommendation but only 8%

of adolescents met this goal and fewer than 5% of adults met the 30 minutes or more per day recommendation. These estimates of physical activity participation are substantially lower than those obtained in nationally representative surveys by self-report described above. The reasons for the differences are not clear. One reason may be participant over-estimation of physical activity in self-report surveys. Alternatively, accelerometers may not be accurately capturing all reported physical activity for a variety of reasons. Most likely, some combination of reasons explain the disparity. A much better understanding of how objective physical activity measurements obtained with currently available and new instrumentation relate to a variety of health outcomes is needed before such measurements can be used to inform future physical activity recommendations and policy statements.

Development of Physical Activity Guidelines in the United States[1]

By the late 1960s, a number of individuals and organizations in the United States had recognized the increasingly sedentary nature of the population and the negative health and fitness consequences of this decline in activity, and were promoting their own interpretation of a good or best exercise program. Data from a growing number of observational and experimental studies supported the value of being physically active, but no consensus existed on what programs were most effective and safe. Also, during the early 1960s, death rates from coronary heart disease were still on the rise and few effective treatments for preventing sudden cardiac death were available. It was well established that the increased work of the heart during vigorous exercise could trigger cardiac arrest or myocardial infarction in persons with coronary atherosclerosis. However, investigators and clinicians lacked an understanding of the etiology of the atherothrombotic disease process, how to detect it in at-risk populations, and what types and intensities of exercise were safe. Many people, including physicians, were very concerned about adults older than age 45 years increasing their physical activity, especially starting a vigorous exercise program or participating in athletic competition. It was this combination of concern about the need to promote exercise, but at the same time, fear that promoting exercise, if not carefully controlled, would cause many people to experience sudden cardiac death that precipitated the development of the first physical activity guidelines and recommendations. The evolution of the guideline process over a 35-year period has been characterized by attempts to reduce risk while maximizing benefit by providing clinically-oriented recommendations for patient or "at-risk" populations and by public health-oriented recommendations for the general public.

[1] This overview of the development of physical activity guidelines in the United States was adapted from a chapter prepared by W. Haskell for *Epidemiologic Methods in Physical Activity* (15). Its use in this report was approved by the publisher.

Early Development of Physical Activity Recommendations and Guidelines

By the early 1970s, data from several epidemiologic and experimental studies demonstrated that physically active persons, including patients with coronary heart disease (CHD), had better health outcomes than did their less active counterparts. These data were useful in preparing early guidelines because the major concern was how to minimize risk while achieving health benefits. The earliest such guidelines were published by the American Heart Association (AHA) in 1972 and 1975. The first publication was *Exercise Testing and Training of Apparently Healthy Individuals: A Handbook for Physicians* (16). These guidelines were directed more at reducing the cardiovascular risk imposed by performing moderate- to vigorous-intensity exercise, including exercise testing for the "coronary prone," than at providing information on how to help patients become more physically active. The authors indicated that available data supported exercise in the rehabilitation of patients with CHD, but data were still inadequate to support widespread promotion of exercise for the prevention of CHD. The authors also advised that the exercise recommendations for the healthy but sedentary person, particularly for the middle-aged male, "not be arbitrarily formulated" and that "exercise intensity must be adjusted to individual capacity at the beginning of the program and regulated periodically during the succeeding stages."

The AHA's second publication, *Exercise Testing and Training of Individuals with Heart Disease or at High Risk for its Development: A Handbook for Physicians*, also focused more on assessment of exercise capacity and issues of risk than on details of program implementation, and more on rehabilitation than on secondary prevention (17). The following quote from the publication is an indication of the clinical approach taken to exercise guidelines in the 1970s: "Exercise is a therapeutic agent designed to promote a beneficial clinical effect and, as such, has specific indications and contraindications and possible toxic or adverse reactions" (page 24).

During this same time period, several professional organizations and government agencies began to issue recommendations, guidelines, and position stands on the importance of being physically active, how much of what types of activity should be performed, and how best to implement a safe activity plan to increase health and fitness. In 1973, *Exercise and Sport Sciences Reviews* published "The Quantification of Exercise Training Programs," a review of research on endurance exercise training and cardiorespiratory fitness by Michael Pollock (18). Much of the information developed during this review was used by Pollock and colleagues as the scientific basis for the first American College of Sports Medicine (ACSM) Position Statement on "The Recommended Quantity and Quality of Exercise for Developing and Maintaining Fitness in Healthy Adults," which was published in 1978 (19). This Position Statement focused on "developing and maintaining cardiorespiratory fitness and body composition in healthy adults," and its key recommendations were that individuals perform an endurance-type activity for 15 to 60 minutes, 3 to 5 days per week, at 60% to 90% of heart rate reserve or 50% to 85% of maximal oxygen uptake. Although reasonably brief (2.5 pages of text and 90 references), the recommendations in this document became the mainstay for most exercise professionals and much of the public wanting to know, "How much exercise is enough?" It is worthwhile noting that all the references cited in this document were from the field of exercise physiology, with none from physical activity or behavioral epidemiology.

The ACSM reissued this Position Stand in 1990 and changed the title to "The Recommended Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory and Muscular Fitness in Healthy Adults" (20). The dose of exercise recommended was quite similar to the 1978 recommendation, with frequency and exercise mode remaining the same, session duration changing from "15 to 60" minutes to "20 to 60" minutes, and intensity changing from "60% to 90% of heart rate reserve or 50% to 85% of maximal oxygen uptake" to "60% to 90% of maximum heart rate or 50% to 85% of maximal oxygen uptake or heart rate reserve." A specific recommendation for enhancing muscle strength was added: one set of 8 to 12 repetitions of 8 exercises, 2 days per week. The statement also indicated that less intensive exercise might also provide health benefits: "ACSM recognizes the potential health benefits of regular exercise performed more frequently and for a longer duration, but at lower intensities than presented in this position statement." (p. 266).

In 1998, the ACSM published the third edition of its Position Stand, entitled, "Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory and Muscular Fitness, and Flexibility in Healthy Adults" (21). The primary recommendations for exercise to enhance cardiorespiratory and body composition remained similar to the 1978 and 1990 recommendations except for a small reduction at the low end of the intensity range: 55% to 90% of maximum heart rate instead of 60% to 90% or 40% to 85% of maximal oxygen uptake reserve or heart rate reserve instead of 50% to 85%. This 1998 document also included recommendations for flexibility and adopted the concept of accumulation from public health recommendations published by the Centers for Disease Control and Prevention (CDC) and ACSM in 1995 (8). (See the following section for more details on the 1995 CDC/ACSM recommendations.) In discussing "duration of training, the ACSM Position Stand recommended "20 to 60 minutes of continuous or intermittent (minimum of 10-minute bouts accumulated throughout the day) of aerobic activity."

In addition to these Position Stands, the ACSM as well as other organizations developed publications that provided detailed guidelines for specialists such as physicians, exercise scientists, physical educators, physical therapists, coaches, and nurses. These guidelines were intended for use in providing exercise and fitness evaluations, developing physical activity prescriptions or plans for individuals or groups, and providing exercise instruction or leadership for patients and healthy persons. Included in these documents were the 7 editions of *Guidelines for Exercise Testing and Exercise Prescription* published by the ACSM between 1975 and 2005 (10;22-27) and *Exercise Standards: A Statement for Healthcare Professionals from the American Heart Association* (28).

A Paradigm Shift to Public Health Physical Activity Guidelines

Starting in the mid-1980s, various medical and public health organizations held discussions and published manuscripts on public health rather than clinical approaches to physical activity for achieving improved health outcomes (29). For example, CDC's Behavioral Epidemiology and Evaluation Branch organized a "Workshop on the Epidemiological and Public Health Aspects of Physical Activity and Exercise" in 1984, in which experts reviewed the current knowledge base relating physical activity to health status and identified actions to be taken to increase the activity status of Americans (30). Ten manuscripts were prepared as the basis for discussion during the conference, and they were published along with a conference overview (31). This meeting played a significant role in setting the stage for the evolution of a public health paradigm for physical activity over the next decade.

The goal of this effort was to augment or supplement, but not necessarily replace, the existing exercise-for–fitness paradigm promoted by the ACSM and other organizations by focusing primarily on enhancing physical fitness or working capacity, either in healthy persons or in the rehabilitation of various patient populations (32). During this 10-year period, substantial new data were published, especially from physical activity epidemiology, which related inactivity to increased risk of several chronic diseases and the potential protective effects of moderate-intensity, as well as vigorous-intensity activity. In addition, researchers reconsidered some of the prior epidemiologic data with respect to the most likely kinds and patterns of physical activity that were carried out by active people, who comprised some of the lower-risk groups. The tentative conclusion was that much of this risk-reducing activity was of moderate intensity (usually considered 3.0 to 6.0 METs) and that it was frequently performed in repeated short bouts. Thus, a disconnect appeared to exist between the accepted exercise-fitness paradigm, which emphasized vigorous activity performed in bouts of at least 20 minutes duration, and the intensity and bout duration that appeared to provide some protection against selected chronic diseases and all-cause mortality.

For example, the results of some studies indicated that regular walking or other moderate-intensity activity, or moderate levels of cardiorespiratory fitness, were associated with reduced rates of cardiovascular disease (CVD) and all-cause mortality (4;33;34). Also, an increasing number of experimental studies showed disease risk factors or health-related fitness measures to be significantly improved in sedentary adults as a result of adherence to a program of regular walking or other moderate-intensity activity (35-37). During this time, a team of Canadian exercise scientists organized two major international conferences on Exercise, Fitness and Health (38) and Physical Activity, Fitness and Health (39). For both conferences, the goal was to understand the relationship of physical activity and fitness to major health outcomes, develop a conceptual model for these relationships, and formulate a consensus statement. These conferences and publications provided an excellent resource for the developing consensus that a physically inactive lifestyle is a major contributor to poor health outcomes throughout the lifespan.

In 1992, in light of the mounting evidence that a sedentary lifestyle significantly increased the risk of CHD morbidity and mortality, the AHA made sedentary lifestyle its fourth major CHD risk factor, joining cigarette smoking, hypertension, and hypercholesterolemia (40). This statement was the first formal recognition by the AHA that physical inactivity was a major independent risk factor for atherosclerotic heart disease and that physical activity could play a role in both primary and secondary prevention of CHD. This document went beyond recognizing just the benefits of exercise for heart disease to stating that people of all ages could benefit from a regular exercise program. It noted that activities such as walking, hiking, swimming, cycling, tennis, and basketball were especially beneficial if performed at 50% or more of a person's work capacity and that even low-intensity activities performed daily could have some long-term health benefits. This statement has been updated over the years by the AHA but without major changes in the key statements made in 1992; the most recent update was published in 2003 (41).

Given the influential nature of official position statements or recommendations by the AHA on heart disease prevention and treatment practices by the medical community in the United States, the elevation of inactivity to a major CHD risk factor brought substantial attention to the importance of a physically active lifestyle. Although this statement indicated the general nature of the activity that should be performed to help maintain good health, it lacked specific details regarding program design and implementation. However, it did indicate that intensities lower than that generally promoted in the past could provide health benefits.

In 1993, the year following the AHA statement recognizing inactivity as a major CHD risk factor, the CDC in collaboration with the ACSM, began developing a document that would provide specific recommendations about the profile of physical activity that should be performed to promote good health. To develop this statement, an expert panel was appointed that consisted of epidemiologists, exercise physiologists, public health professionals, and health psychologists. The panel was charged with developing a statement grounded in solid science that would clearly communicate its key messages to the public and provide a program that could be performed by a large segment of the general public with a minimal increase in risk. It took 2 years of work by the panel before *Physical Activity and Public Health: A Recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine* was released to the public in 1995 (8). These first public health guidelines on physical activity and health were the culmination of a decade of work that began in 1984 with the CDC Workshop on the Epidemiological and Public Health Aspects of Physical Activity and Exercise.

The approach to physical activity for health taken by these ”public health” guidelines was quite different than prior guidelines primarily based on the “exercise training” or “clinical” paradigm. The primary recommendation was that “Every American adult should accumulate 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week.” Because many of the prior recommendations had primarily advocated vigorous-intensity activity, having moderate-intensity activity as the key recommendation (even though prior guidelines based on vigorous-intensity exercise were recognized as still effective) raised many questions by exercise scientists and practitioners. The idea that substantial health benefits could be derived from brisk walking was not appreciated by many fitness advocates, but this recommendation was based on data from a variety of epidemiologic and experimental studies. Even more controversial was the idea that the activity each day did not need to be performed continuously for at least 30 minutes, but could be *accumulated* throughout the day in bouts of 8 to 10 minutes. For many years, the idea that the activity needed to be continuous to be effective had been promoted in programs such as "Aerobics" (42) but without any scientific evaluation. In retrospect, the recommendation for accumulated bouts appears to have been correct. However, in 1995, the published scientific data supporting this concept was quite limited, and remains so today. Only several experimental studies had directly compared the effects of continuous exercise bouts versus exercise accumulated through bouts of 8 to 10 minutes duration (43-45), and the nature of data collection in epidemiologic studies made the evaluation of the accumulation concept difficult, at best, to evaluate.

Following close on the heels of the CDC/ACSM report, the National Institutes of Health (NIH) convened a consensus conference on "Physical Activity and Cardiovascular Health" (46). The charge to this nonfederal, non-advocate 13-member panel representing cardiology, psychology, exercise physiology, nutrition, pediatrics, public health and epidemiology was "to provide physicians and the general public with a responsible assessment of the relationship between physical activity and cardiovascular health." During the 3-day conference, the panel listened to reports from 27 scientists on the relationship between physical activity and cardiovascular health, had open discussions with the presenting scientists and others in attendance, and held closed deliberations to formulate their recommendations. The draft recommendations were shared with conference participants and conflicting views were resolved and a final document produced.

The panel concluded that: (1) most Americans have little or no physical activity in their daily lives; (2) accumulating evidence indicates that physical inactivity is a major risk factor for cardiovascular disease; (3) moderate levels of physical activity confer significant health benefits; (4) all Americans should engage in regular physical activity at a level appropriate to their capacity, needs and interests; and (5) children and adults should set a goal of accumulating at least 30 minutes of moderate intensity physical activity on most, and preferably all, days of the week.

The panel also recognized that a greater amount and/or intensity of activity than the recommended minimum would provide greater health benefits for most people (i.e., dose response) and that cardiac patients should integrate increased physical activity into a comprehensive program of risk reduction. Thus, the panel made recommendations highly consistent with the CDC/ACSM working group in that it emphasized performing moderate-intensity physical activity (using brisk walking as a benchmark) on most or all days for at least 30 minutes per day, and noted the activity could be accumulated in bouts of at least 8 to 10 minutes duration. It also recognized that its recommendation was a minimum, and greater health benefits were achievable by performing greater amounts of activity or through "vigorous exercise." In other words, the prior recommendations of vigorous exercise performed for 20 to 30 minutes 3 days per week still applied.

At the same time the NIH was producing its consensus panel report, the World Health Organization also issued a report on the health benefits of regular activity (47). The major recommendations in this document were very consistent with recommendations made by the CDC/ACSM working group and the NIH consensus panel, namely that a target for all adults should be 30 minutes or more of moderate-intensity physical activity on most days. The WHO report also stated that daily physical activity should be the cornerstone for a healthy lifestyle throughout the lifespan; that more vigorous exercise, such as slow jogging, cycling, field and court games, and swimming, could provide additional health benefits; and that people with disabilities or chronic disease had a great deal to benefit from an individualized activity program. While recognizing that the responsibility for personal health decisions ultimately lies with the individual and family, policy recommendations for increasing physical activity were included in the report as well for major government organizations.

The CDC/ACSM, NIH, and WHO reports on physical activity and health, all published in 1995 and 1996, set the stage for the publication of *Physical Activity and Health: A Report of the Surgeon General* in 1996 (11). This report was commissioned by the Secretary of Health and Human Services in 1994 and authorized the CDC to be the lead agency for its development with collaboration from a number of federal organizations, especially the President's Council on Physical Fitness and Sports and the NIH. Non-government collaborating organizations included the ACSM, AHA, and the American Association of Health, Physical Education, Recreation and Dance. This was an extensive undertaking, and approximately 195 people contributed to writing, editing, reviewing, and publishing the report.

The stated goal of the Surgeon General's report was to summarize the existing literature on the role of physical activity in preventing disease and on the status of interventions to increase physical activity. It provided an historical background on the relation of physical activity to health, including the evolution of physical activity guidelines, looked at patterns and trends of physical activity in different populations in the United States, and described various projects to promote increased physical activity in youth and adults. It also summarized information on acute and chronic physiological responses to exercise and provided a systematic review of the effects of physical activity on major health outcomes. The report grew out of an emerging consensus among investigators and providers working in exercise science, epidemiology, public health, clinical medicine, health psychology, and education that the high prevalence of sedentary behavior among the American population was having a significant negative health impact, that a moderate amount and intensity of physical activity in this sedentary population could provide important health benefits, and that innovative, long-term programs were needed to reverse the continuing downward trend in physical activity.

The key recommendation from the Surgeon General's report was that people of all ages could improve the quality of their lives through a lifelong practice of moderate-intensity physical activity: "A regular, preferably daily, regimen of at least 30 to 45 minutes of brisk walking, bicycling, or even working around the house or yard will reduce the risk of coronary heart disease, hypertension, colon cancer and diabetes." A second key message was that "more is better." People already performing a moderate level of activity would benefit even more by increasing the intensity and/or duration of their activity. Both the CDC/ACSM report and the report by the Surgeon General have been cited frequently in the professional literature on physical activity and health, and the key recommendations, usually with no or only minor modifications, have been adopted by national agencies in a number of other countries.

To help assess the information available on the dose of physical activity needed for specific health outcomes, an international "consensus symposium" was held at Hockley Valley, Ontario, Canada in 2000 (48). The goal of this evidence-based symposium was to provide a comprehensive review of the existing science relating physical activity dose to health and to make specific recommendations regarding physical activity dose. The major conclusion regarding the dose-response relation for specific outcomes was that the available data were still inadequate to define any precise relation. However, the consensus panel did endorse the recommendations made in the CDC/ACSM report (8) and the Surgeon General's report (11).

The Institute of Medicine Report

In 2002, the Institute of Medicine (IOM) published a report primarily focusing on macronutrient intake and energy intake and expenditure. The report developed estimates of daily intake that are compatible with good nutrition throughout the life span and that may decrease the risk for chronic disease (49). The preparation of this report by the IOM, a private nonprofit organization and component of the National Academy of Sciences, was funded by HHS, the US Department of Agriculture (USDA), the US Department of Defense, and Health Canada. The panel considered the level of macronutrient, and thus caloric intake, consistent with good health and the caloric expenditure needed to keep people in a healthy weight range, defined as a body mass index (BMI) of 18.5 to 25.0 kg/m^2. For people to achieve these goals, the panel concluded the following regarding physical activity:

"Physical activity promotes health and vigor. Cross-sectional data from a doubly labeled water database were used to define a recommended level of physical activity, based on the physical activity level (PAL) associated with a normal body mass index (BMI) range of 18.5 to 25 kg/m^2. In addition to the activities identified with a sedentary lifestyle, an average of 60 minutes of daily moderate intensity physical activity (e.g., walking/jogging at 3 to 4 miles/hour) or shorter periods of more vigorous exertion (e.g., jogging for 30 minutes at 5.5 miles/hour) was associated with a normal BMI and therefore is recommended for normal-weight individuals. This amount of physical activity leads to an 'active' lifestyle, corresponding to a PAL greater than 1.6 (see Chapter 5). Because the Dietary Reference

Intakes are provided for the general healthy population, recommended levels of physical activity for weight loss of obese individuals are not provided." (p.880).

Upon the release of this report, many in the press, general public, and health professions considered that the report had articulated a significant change in physical activity recommendations for health, with the target now being 60 minutes of moderate-intensity activity daily rather the 30 minutes or more that had been promoted since 1995. However, it is very important to understand that the prior recommendations by CDC, ACSM, NIH, and HHS were based primarily on the amount of physical activity shown to be consistent with lower morbidity and mortality rates from selected chronic diseases and all-cause mortality, and not on the amount for achieving an optimal BMI of 18.5-25.0 kg/m^2, which was the major goal of the IOM report. Also, in the IOM report, the 60-minute recommendation was made in order to achieve *all* the identified health benefits fully, while in the other reports, the 30 or more-minute recommendation was considered a minimum. The other reports acknowledged that more exercise would bring additional benefits. As with the prior reports, the IOM document indicated that activity could be accumulated throughout the day and did not need to be performed only in a single session.

A key difference in the data considered during the formulation of the IOM recommendation versus other previous physical activity recommendations was the IOM panel's emphasis on doubly-labeled water studies. Combining data from available doubly-labeled water studies, the panel estimated the total daily energy expenditure of men and women who had a BMI of 18.5 to 25.0 kg/m^2. They determined that these subjects had an average PAL of about 1.75. The panel then took the PAL of people considered to be sedentary (1.25) and that of people considered to be of normal weight (1.75) then calculated the difference in PAL between people who were sedentary and those who were normal weight and converted this to minutes per day of moderate-intensity activity. Not taken into this consideration was the fact that the PAL for the subjects in the doubly-labeled water studies who were overweight or obese was not 1.25 but in the 1.59 to 1.85 range (50). These cross-sectional data do not deal with the question of how much added exercise will produce a meaningful change in body weight.

The IOM selection of a target activity level of 60 minutes per day or a PAL of 1.6 or greater to maintain optimal body weight is somewhat less than the target PAL of 1.75 in the 1998 report by the World Health Organization, *Obesity: Preventing and Managing the Global Epidemic* (51). In this extensive report, the authors stated that analyses of more than 40 national physical activity studies worldwide show a significant relationship between the average BMI of adult men and their PAL, with the likelihood of becoming overweight being substantially reduced at PALs of 1.8 or above. For women, the PAL associated with a healthy weight was approximately 1.6. Therefore, the WHO report suggested "that people should remain physically active throughout life and sustain a PAL of 1.75 or more in order to avoid excessive weight gain" (p.124).

In 2002, an international group of scientists with expertise in physical activity, nutrition, energy balance and obesity held a consensus meeting convened by the International Association for the Study of Obesity to assess "how much physical activity is enough to prevent unhealthy weight gain" (52). Part of their conclusion was that, "The current physical activity guideline for adults of 30 minutes of moderate intensity activity daily, preferably all days of the week, is of importance for limiting health risks for a number of chronic diseases, including coronary heart disease and diabetes. However, for the prevention of weight gain or regain this guideline is likely to be insufficient for many individuals in the current environment. There is compelling evidence that prevention of weight regain in formally obese individuals requires 60 to 90 minutes of moderate intensity activity or lesser amounts of vigorous activity. Although definitive data are lacking, it seems likely that moderate intensity activity of approximately 45 to 60 minutes per day or 1.7 PAL is required to prevent the transition to overweight or obesity" (page 101). This consensus statement recognized that the amount of physical activity associated with lower chronic disease mortality rates is very likely less than that needed in the current environment to prevent unhealthy weight gain or regain in many adults.

Dietary Guidelines for Americans, 2005

Every 5 years, the USDA and HHS are required by the US Congress to prepare *Dietary Guidelines for Americans*. The Guidelines published in 1995 and 2000 recognized that a physically active lifestyle should be maintained for optimal health, but no specific guideline focused on prevention of weight gain or weight loss. For example, in 2000 the recommendations were highly consistent with the 1995 CDC/ACSM report directed to improving general health status: "Aim to accumulate at least 30 minutes (adults) or 60 minutes (children) of moderate intensity activity on most days of the week, preferably daily. If you already get 30 minutes of physical activity daily, you can gain even more health benefits by increasing the amount of time you are physically active or by taking part in more vigorous activities. No matter what activity you choose, you can do it all at once, or spread it out over two or three times per day" (53), p.10.

The 2005 *Dietary Guidelines for Americans* structured the physical activity recommendations to separate advice about chronic disease prevention from advice about the amount of physical activity required for the prevention of unhealthy weight gain or regain or achieving weight loss in adults (54). They took the generally accepted position that a variety of health benefits are derived from at least 30 minutes of moderate-intensity exercise on most days, and separated this recommendation from the less well documented and understood recommendations regarding the amount of physical activity required to prevent unhealthy weight gain or regain and weight loss. The physical activity recommendations needed to help manage body weight were adopted in large part from the 2002 IOM report (49), which had primarily considered cross-sectional data from doubly-labeled water studies of energy expenditure (55). To help adults manage body weight and prevent gradual unhealthy weight gain, the *Guidelines* recommended approximately 60 minutes of moderate/vigorous activity on most days of the week (while not exceeding calorie requirements). To help adults lose weight and to sustain weight loss, the *Guidelines* recommended at least 60 to 90 minutes of daily moderate-intensity physical activity daily (while not exceeding calorie requirements). These two recommendations regarding weight gain prevention and weight loss received the most attention and contributed to some confusion among the public.

2007 American College of Sports Medicine and American Heart Association Physical Activity Recommendations

In 2002, the ACSM and CDC organized an expert panel to consider whether the 1995 CDC/ACSM physical activity and public health recommendations needed to be updated (8). Key reasons for this consideration included new scientific evidence since 1995 relating physical activity to health, physical activity recommendations by various organizations in the interim that appeared to be in conflict with the 1995 recommendations, and communications issues related to certain terminology used in the 1995 report. The panel decided that an update would be of value to health professionals and the public, and two writing groups were formed, one to prepare recommendations for adults (18 to 65 years) and another for older adults (older than 65 years). The purpose of these reports was to update and clarify the 1995 recommendations on the types and amounts of physical activity needed by healthy adults and older adults to improve and maintain health. These groups reviewed advances in pertinent physiologic, epidemiologic, and clinical scientific data, including primary research articles and reviews published since the original recommendation was issued in 1995.

The writing groups prepared the two manuscripts, intending that the recommendations would represent an update from CDC and ACSM. However, after extensive review at CDC and HHS, it was decided that because physical activity recommendations for adults had been published as part of the 2005 *Dietary Guidelines for Americans* that CDC should not issue additional physical activity recommendations. ACSM representatives then asked the AHA to participate in issuing the updated recommendations, and the two sets of recommendations were published in 2007 (56;57). No major changes were made in the recommendations either for adults or older adults but a number of features about the type and amount of activity most likely to provide various benefits were clarified. Also, issues regarding the role of physical activity in body weight management were addressed and resistance exercise was made part of the core recommendation for all adults.

Primary recommendations for adults included the following:

- To promote and maintain health, all healthy adults aged 18 to 65 years need moderate-intensity aerobic (endurance) physical activity for a minimum of 30 minutes on 5 days each week or vigorous-intensity aerobic physical activity for a minimum of 20 minutes on 3 days each week. Combinations of moderate- and vigorous-intensity activity can be performed to meet this recommendation. For example, a person can meet the recommendation by walking briskly for 30 minutes twice during the week and then jogging for 20 minutes on 2 other days. Moderate-intensity aerobic activity, which is generally equivalent to a brisk walk and noticeably accelerates the heart rate, can be accumulated toward the 30-minute minimum by performing bouts each lasting 10 or more minutes. Vigorous-intensity activity is exemplified by jogging, and causes rapid breathing and a substantial increase in heart rate.

- In addition, every adult should perform activities that maintain or increase muscular strength and endurance a minimum of 2 days each week. Because of the dose-response relation between physical activity and health, persons who wish to further improve their personal fitness, reduce their risk for chronic diseases and disabilities or prevent unhealthy weight gain may benefit by exceeding the minimum recommended amounts of physical activity.

The recommendations for older adults are very similar to the updated ACSM/AHA recommendations for adults, but have several important differences. For example, the recommended intensity of aerobic activity takes into account the older adult's aerobic fitness, activities that maintain or increase flexibility are recommended, and balance exercises are recommended for older adults at risk of falls. In addition, older adults are encouraged to have an activity plan for achieving recommended physical activity that integrates preventive and therapeutic recommendations. The promotion of physical activity in older adults places more emphasis on moderate-intensity aerobic activity, muscle-strengthening activity, reducing sedentary behavior, and risk management.

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Part E: Integration and Summary of the Science

Introduction

The PAGAC's final step in developing this report was to integrate and summarize the key conclusions and supporting data that each subcommittee prepared and presented in their chapters (***Part G: The Science Base***). Each chapter in ***Part G*** provides a review of the scientific literature on physical activity and a selected health outcome or population, and the chapters' conclusions are supported by original publications cited in extensive reference lists.

Each subcommittee's major conclusions were reviewed and accepted by the PAGAC during its final meeting on February 28-29, 2008. Because much of the scientific review by PAGAC members and consultants was organized around specific health outcomes, the PAGAC decided that it needed, where possible, to integrate key findings for these various outcomes into general statements about the scientific support for health-related benefits of physical activity. This chapter provides the results of the Committee's summary and integration process. Using a plan outlined below, PAGAC members first summarized the type and strength of evidence for their major conclusions. This evidence is presented in a series of tables on **pages E-4 to E-22**

The Committee then integrated the evidence and conclusions by developing responses to a set of questions that are typical of those raised by health and fitness professionals and the general public about the scientific evidence on a number of issues about physical activity and health. These responses are supported by the information provided in the chapters in ***Part G: The Science Base***. The questions and answers can be found on **pages E-22 to E-35**.

Summarizing the Evidence

During the final PAGAC meeting, each subcommittee chair was asked to prepare a summary of key findings for discussion by the Committee, using the plan outlined in Table E.1. Each subcommittee's summary report was to include information on the type and magnitude of evidence reviewed, the strength of the evidence, characteristics of the physical activity most likely to produce the outcome, any evidence of a dose response, and any evidence that being sedentary puts a person at high risk (see Table E.1A). To determine the overall strength of the evidence for major health and fitness outcomes and to evaluate the issue of dose response for these outcomes, subcommittees considered the types of studies that addressed each specific question (see Table E.1B) and the general quality of these studies (e.g., design, sample size, statistical power, measurement methods, follow-up, adherence). For each major outcome, but not for each study, subcommittee chairs were asked to assign a strength of evidence — strong, moderate, weak — based on the evidence they included in their review chapters (see Table E.1C). Also, in assigning the strength of the evidence, subcommittees included factors that support a causal relation between physical activity and a specific outcome, such as evidence of favorable changes in biomarkers considered to be in the causal pathway or a significant dose-response relation.

Table E.1. Process for Summarizing the Science

A. Instructions to Subcommittee Chairs

- Only major outcomes to be considered in summary
- Types and amounts of evidence available for this outcome
- Strength of the evidence (strong, moderate, weak)
- Based on current science characteristics of activity most likely to produce this outcome
    - *Type: aerobic, resistance, other*
    - *Intensity: light, moderate, vigorous (include comment on walking)*
    - *Frequency: times per week*
    - *Duration; minutes per day/week*
    - *Amount: MET-hours per week (or other measure if appropriate)*
    - *Accumulation: multiple bouts during day*
- Any evidence of dose response for amount or intensity
- Any evidence that being very sedentary puts person at highest risk. If possible, quantify.

B. Types of Evidence

- **Type 1**
    - Randomized controlled trials (RCT) (or meta-analyses) without major limitations
- **Type 2**
    - 2a – RCTs (or meta-analyses) with important limitations
    - *2b – Non-randomized clinical trials*
- **Type 3**
    - 3a – Well-designed prospective cohort studies and case-control studies
    - *3b – Other observational studies, e.g., weak prospective cohort studies or case-control studies; cross-sectional studies or case series*
- **Type 4**
    - *Inadequate, very limited, or no data in population of interest. Anecdotal evidence or no/little clinical experience*

C. Strength of the Evidence

- Strong, consistent across studies and populations
- Moderate or reasonable, reasonably consistent
- Weak or limited, inconsistent across studies and populations

While deciding on a plan for summarizing the evidence, PAGAC members discussed the possible use of an evidence-based rating system designed for the development of evidence-based guidelines for medical practice, such as those adopted by the American College of Cardiology and the American Heart Association in 2006 (1). This approach was dismissed for several reasons. First, a full application of these methodologies did not apply to the PAGAC mission, which was to review and evaluate the science, not to provide practice guidelines or recommendations. Second, Committee members were concerned that the criteria used to evaluate evidence for the safe and effective use of medical interventions or therapies (such as drugs or medical devices) developed to treat disease are not readily applicable for evaluating the effects of lifestyle changes on chronic disease prevention, where standards of experimental design such as double blinding are exceptionally difficult, if not impossible.

The Committee also recognized that because of logistical, cost, and ethical issues, few RCTs have been conducted to link physical activity to reduced rates of chronic diseases. This situation is not very different from that linking other health-related behaviors to the prevention of clinical outcomes. A good example is cigarette smoking. For obvious ethical reasons, no one has conducted an RCT of the impact of starting cigarette smoking on health outcomes, such as lung cancer, chronic obstructive pulmonary disease, or coronary heart disease. A similar situation exists for the relation between saturated fat or trans-fatty acid intake and the prevention of coronary heart disease. Yet, the weight of evidence is believed to be so strong from observational studies that urging the public to stop smoking or reduce their intake of saturated fat or trans-fatty acids are major components of national public health campaigns. Similarly, data linking physical activity to lower rates of all-cause mortality, coronary heart disease, stroke, and type 2 diabetes based on observational studies are strong and, further, are supported by RCTs showing significant favorable effects on key biomarkers for these conditions. The result of these deliberations by the PAGAC was the development of the evidence rating criteria presented in Table E-1.

Selected PAGAC members were then asked to integrate the main conclusions from these subcommittee summaries under the headings of youth, adults, older adults, understudied populations, and adverse events. These summary conclusions were presented to PAGAC members, and each set of conclusions was discussed and edited. A final set of conclusions was developed using a consensus process.

Following the PAGAC meeting on February 28-29, 2008, the Committee prepared the following information, which summarizes the major conclusions of each committee. The sum of the evidence provided here for a wide range of health and fitness outcomes strongly supports the value of being physically active versus being sedentary throughout the lifespan.

Health Outcome: All-Cause Mortality
Types of studies? Type 3a – extensive
What is the nature of the association of physical activity (PA) with All-Cause Mortality? There is a clear inverse relationship between PA and all-cause mortality. Strength of evidence: Strong
What is the effect size? There is about a 30% risk reduction across all studies, comparing most with least active subjects. Strength of evidence: Strong
Is there any evidence for an effect of sex, age, or race/ethnicity? There is evidence that this association exists for both men and women, as well as for people both younger than age 65 years or 65 years of age and older. There is also evidence that this association exists for different race/ethnic groups. Strength of evidence: Sex = Strong, <65 & 65+ years = Strong, Race/Ethnicity = Reasonable
Is there a dose-response effect? There is an inverse dose-response relation for total volume of PA (i.e., total energy expenditure). The shape of the dose-response curve appears curvilinear in that larger risk decreases are seen at the lower end of the physical activity spectrum than at the upper end. There are limited data on an inverse dose-response relation for intensity, which is independent of its contribution to the total volume of PA (i.e., limited data suggest that vigorous physical activity may be associated with further risk reduction compared with moderate-intensity activity when the total volume of energy expenditure is the same). Strength of evidence: Volume = Strong, Intensity = Limited
What is an effective PA dose regarding mode, duration, intensity, and frequency that is supported by the evidence? (Strength of evidence in parentheses) Data indicate at least 2 to 2.5 hours per week of moderate-to-vigorous physical activity are needed to see significantly lower risk (Strong). Data are primarily for aerobic leisure-time physical activity (LTPA) (Strong). There are also specific data showing that walking at least 2 hours per week is associated with significantly lower risk (Strong). Some evidence also indicates that all activities count (Reasonable) This amount — 2 to 2.5 hours per week of moderate-to-vigorous PA — does not represent a threshold level for risk reduction. The data consistently support a “some is good; more is better” message (Strong). Some data indicate that among populations where physical activity levels are likely to be low (e.g., middle-aged and older women; older men), significantly lower mortality rates are observed at levels less than 2 to 2.5 hours per week of moderate-to-vigorous PA (Limited).

Health Outcome: All-Cause Mortality (continued)
What is the evidence on accumulation? (Strength of evidence in parentheses) No direct data on multiple short bouts versus one long bout. However, indirect data come from epidemiologic studies showing an inverse association with total volume, where the PA is likely to be accumulated from activities of different (but unknown) durations (Reasonable).
What other unique comments should be made about the evidence of PA with this health outcome? (Strength of evidence in parentheses) The association of PA and all-cause mortality is independent of body mass index (Strong); this association is seen regardless of whether persons are normal weight, overweight, or obese (Reasonable).

Health Outcome: Cardiorespiratory Health
Types of studies? Type 3a – extensive for coronary heart disease (CHD), cardiovascular disease (CVD), and stroke Type 1 – extensive for hypertension, atherogenic dyslipidemia, and cardiorespiratory fitness
What is the nature of the association of PA with Cardiorespiratory Health? There is a clear inverse relation between PA and cardiorespiratory health (CHD, CVD, stroke, hypertension, and atherogenic dyslipidemia). The data imply relations with physical activity volume, with less information about intensity and none for frequency and duration per session for CVD clinical events. Physical activity improves cardiorespiratory fitness. Fitness has direct dose-response relations between intensity, frequency, duration, and volume. There is limited evidence for an accumulation effect. Strength of evidence: Strong
What is the effect size? There is a 20% to 35% lower risk for CVD, CHD, and stroke. Participation in aerobic activity improves cardiorespiratory fitness in a dose-response fashion according to the frequency, duration, intensity, and total volume of the exposure. Percentage increases are highly dependent on fitness levels at baseline, sex, and age of the study population, and range from 4.5% with low-volume brisk walking to close to 20% with high-volume, high-intensity exercise training. Strength of evidence: Strong
Is there any evidence for an effect of sex, age, race/ethnicity? These associations exist for both men and women and individuals of all ages. There is no evidence for sex-specific, age-specific, or race/ethnic specific effects when volume is the exposure rather than relative intensity. Strength of evidence: Sex = Strong, Age = Strong, Race/Ethnicity = Reasonable

Health Outcome: Cardiorespiratory Health (continued)
Is there a dose-response effect? There is a dose-response relation for CVD and CHD. There appears to be an L-shaped relation for stroke. The relations are all most closely related to volume, with less information about intensity and none for frequency and duration of sessions. Minutes per week is a less powerful parameter of dose response than is volume per week (kilocalories per week; MET-minutes per week). Physical activity improves cardiorespiratory fitness. For fitness there are direct dose-response relations between intensity, frequency, duration, and volume. There is mixed evidence for an accumulation effect. Strength of evidence: Strong
What is an effective physical activity dose regarding mode, duration, intensity, and frequency that is supported by the evidence? (Strength of evidence in parentheses) At least 800 MET-minutes per week or 12 miles per week (moderate and/or vigorous); includes specific data on brisk walking at least 2 hours per week (Strong). Data are primarily for aerobic LTPA (Strong) on top of usual activities of daily living. Risk reductions start to be seen at levels below 800 MET-minutes per week or 12 miles week (Reasonable).
What is the evidence on accumulation? Very limited and mixed data available and mostly for cardiorespiratory fitness. Sparse evidence for other CRH outcomes. Strength of evidence: Limited
What other unique comments should be made about the evidence of PA with this health outcome? Notable lack of evidence for frequency, duration, and intensity effects on hard cardiorespiratory health outcomes (CVD, CHD, and stroke) and lack of trial evidence for duration and intensity for cardiovascular risk factors (hypertension and atherogenic dyslipidemia).

Health Outcome: Metabolic Health
Types of studies? Type 2a (small body) and 3a (reasonable body) for type 2 diabetes Type 3a/b (reasonable body) for metabolic syndrome
What is the nature of the association of PA with Metabolic Health? There is a clear inverse relationship between PA and metabolic health, including the prevention of type 2 diabetes and metabolic syndrome. Strength of evidence: Strong
What is the effect size? There is a 30% to 40% lower risk for type 2 diabetes and metabolic syndrome in at least moderately active people compared to sedentary individuals. Strength of evidence: Strong

Health Outcome: Metabolic Health (continued)
Is there any evidence for an effect of sex, age, race/ethnicity? This association exists for both men and women, as well as for older and younger persons. There is reasonable evidence to show the association exists for different race/ethnic groups. Strength of evidence: Sex = Strong, Age = Strong, Race/Ethnicity = Reasonable
Is there a dose-response effect? There is an inverse dose-response association between volume of PA and the development of metabolic syndrome as well as the development of type 2 diabetes. Strength of evidence: Reasonable
What is an effective PA dose regarding: mode, duration, intensity, and frequency that is supported by the evidence? (Strength of evidence in parentheses) Data indicate at least 120 to 150 minutes per week of moderate-to-vigorous PA is needed to see significantly lower risks (Strong). Data are primarily for aerobic LTPA (Strong). Risk reductions start to be seen at levels below the 120 to 150 minutes per week level of PA (Reasonable).
What is the evidence on accumulation? There are limited data on accumulation.
What other unique comments should be made about the evidence of PA with this health outcome? There is limited evidence that PA helps to control HbA1c levels. There is very limited evidence that PA helps to prevent gestational diabetes.

Health Outcome: Energy Balance
Types of studies? ***Weight maintenance (less than 3% change in body weight):*** Type 1, 2, 3a ***Weight loss (at least 5% loss of body weight):*** Type 1 ***Weight maintenance following weight loss:*** Type 2 ***Abdominal obesity:*** Type 1, 2

Health Outcome: Energy Balance (continued)
What is the nature of the association of PA with Energy Balance? (Strength of evidence in parentheses) ***Weight maintenance (less than 3% change in weight):*** There is a favorable and consistent effect of aerobic PA on achieving weight maintenance (Strong). The evidence is less consistent for resistance training, in part, because of the compensatory increase in lean mass (Moderate), and the smaller volumes of exercise employed. ***Weight loss (at least 5% loss of weight):*** The amount of weight lost due to PA (alone) is dependent on the volume of activity, and few studies have used a volume of PA large enough to achieve a 5% weight loss. If an isocaloric diet is maintained throughout the PA intervention, weight loss is similar to what is observed for dietary interventions and clearly exceeds 5% (Strong). ***Weight maintenance following weight loss:*** PA promotes less weight regain after a period of significant weight loss (Moderate). ***Abdominal obesity:*** A decrease in total abdominal adiposity and intra-abdominal adiposity is associated with aerobic PA (Moderate to Strong). The effect is less well described for resistance training (Weak).
What is the effect size? (Strength of evidence in parentheses) ***Weight maintenance (less than 3% change in weight):*** Aerobic PA has a consistent effect on achieving weight maintenance (Strong); resistance training has a moderate effect (Limited). ***Weight loss (at least 5% loss of weight):*** PA alone has no effect on achieving a 5% weight loss, except at very large volumes of PA or when an isocaloric diet is maintained throughout the PA intervention (Strong). ***Weight maintenance following weight loss:*** Aerobic PA has a reasonably consistent effect on weight maintenance following weight loss (Moderate). ***Abdominal obesity:*** Aerobic PA has a consistent effect on total abdominal adiposity and a smaller effect on intra-abdominal adiposity (Strong). Resistance training has a small and less consistent effect on total abdominal and intra-abdominal adiposity (Limited).
Is there any evidence for an effect of sex, age, race/ethnicity? There is some evidence that the amount of physical activity needed to maintain a constant weight differs between men and women and increases with age. However, the evidence is not sufficient to recommend differential physical activity regimens based on sex or on age alone. The paucity of literature, particularly of the stronger longitudinal cohort or randomized controlled intervention study designs, makes it unwise to draw conclusions as to whether the physical activity recommendation should differ by racial/ethnic or socioeconomic status groups. Strength of evidence: Sex = Weak, Age = Weak, Race/Ethnicity = Weak

Health Outcome: Energy Balance (continued)
Is there a dose-response effect? (Strength of evidence in parentheses) ***Weight maintenance (less than 3% change in body weight):*** There is no evidence for a dose-response effect for PA and weight maintenance, as it has not been specifically tested. ***Weight loss:*** There is a clear, consistent dose-response effect of aerobic PA on weight loss (Strong). ***Weight maintenance following weight loss:*** A dose-response is present — those performing the larger volumes of aerobic PA had less weight regain (Moderate). ***Abdominal obesity:*** Larger, well-designed studies report a dose-response relationship for aerobic PA related to abdominal obesity measures (Moderate).
What is an effective PA dose regarding mode, duration, intensity, and frequency that is supported by the evidence? (Strength of evidence in parentheses) ***Weight maintenance (less than 3%):*** The optimal amount of physical activity needed for weight maintenance over the long-term is unclear. However, there is clear evidence that physical activity provides benefit for weight stability. There is a great deal of inter-individual variability with physical activity and weight stability, and many persons may need more than 150 minutes of moderate-intensity activity per week to maintain weight. Data from recent well-designed RCTs lasting up to 12 months indicate that aerobic physical activity performed to achieve a volume of 13 to 26 MET-hours per week is associated with approximately a 1% to 3% weight loss, which is generally considered to represent weight stability. Thirteen MET-hours per week is approximately equivalent to walking at 4 miles per hour for 150 minutes per week or jogging at 6 miles per hour for 75 minutes per week. ***Weight loss (at least 5% weight loss):*** There are clear, consistent data that a large volume of physical activity is needed for weight loss in the absence of concurrent dietary changes. Physical activity equivalent to 26 kilocalories per kilogram (1,560 MET-minutes) or more per week is needed for weight loss of 5% or greater (Moderate); less amounts of weight loss are seen with smaller amounts of physical activity. This relatively high volume of physical activity is equivalent to walking about 45 minutes per day at 4 miles per hour or about 70 minutes per day at 3 miles per hour, or jogging 22 minutes per day at 6 miles per hour. ***Weight maintenance following weight loss:*** PA equivalent to 30 kilocalories per kilogram per week or more. This is equivalent to walking about 50 minutes per day at about 4 miles per hour or 80 minutes per day at about 3 miles per hour, or jogging for 25 minutes per day at 6 miles per hour (Moderate).

Health Outcome: Energy Balance (continued)
Abdominal obesity: Aerobic physical activity in the range of 13 to 26 kilocalories per kilogram per week results in decreases in total and abdominal adiposity that are consistent with improved metabolic function. Thirteen MET-hours per week is approximately equivalent to walking at 4 miles per hour for 150 minutes per week or jogging at 6 miles per hour for 75 minutes per week. However, larger volumes of physical activity (e.g., 42 kilocalories per kilogram per week) result in decreases in intra-abdominal adipose tissue that are 3 to 4 times that seen with 13 to 26 kilocalories per kilogram per week of physical activity.
What is the evidence on accumulation? (Strength of evidence in parentheses) ***Weight maintenance (less than 3%):*** Accumulation of energy expenditure due to PA is what is important to achieving energy balance* (Strong). Accumulation of PA can be obtained in short multiple bouts or one long bout to meet PA expenditure goals for weight maintenance (Moderate). ***Weight loss (at least 5% weight loss):*** There is evidence that accumulation of PA independent of distribution of PA bouts is what is important for weight loss (Limited); however, it is difficult accumulate large volumes of PA without concentrated bouts. ***Weight maintenance following weight loss:*** There is reasonable evidence that accumulation of PA independent of distribution of bouts is what is important for weight stability following weight loss (Limited); however, it is difficult accumulate large volumes of PA without concentrated bouts. ***Abdominal obesity:*** This has not been tested.
What other unique comments should be made about the evidence of PA with this health outcome? *NOTE: It is important to note that the role of energy intake (diet) must be considered in any discussion of physical activity and weight control. Weight loss in excess of 5% can be achieved with large volumes of physical activity. However, a more predictable weight loss occurs when energy intake is held constant during a physical activity intervention.

Health Outcome: Musculoskeletal Health
Types of studies? ***Bone:*** Type 3a: fractures Type 1, 2a: bone density ***Joint:*** Type 3a: prevention and/or promotion of osteoarthritis (OA) Type 1: improvement of OA, rheumatoid arthritis (RA), and fibromyalgia ***Muscular:*** Type 1: muscle strength

Health Outcome: Musculoskeletal Health (continued)
What is the nature of the association of PA with Musculoskeletal Health? (Strength of evidence in parentheses) ***Bone:*** There is an inverse association of PA with relative risk of hip fracture (Moderate) and vertebral fracture (Weak). Increases in exercise training can increase, or minimize the decrease, in spine and hip bone mineral density (BMD) (Moderate). ***Joint:*** In the absence of a major joint injury, there is no evidence that regular moderate PA promotes the development of OA (Moderate). Participation in low/moderate levels of PA may provide a mild degree of protection against the development of OA (Weak, Limited). Participation in moderate-intensity, low-impact PA has disease-specific benefits (pain, function, quality of life, and mental health) for people with OA, RA, and fibromyalgia (Strong). PA may delay the onset of disability in people with OA (Weak). ***Muscular:*** Increases in exercise training enhance skeletal muscle mass, strength, power, and intrinsic neuromuscular activation (Strong).
What is the effect size? (Strength of evidence in parentheses) ***Bone:*** Risk reduction of hip fracture is 36% to 68% at the highest level of PA (Moderate). The magnitude of effect of PA on BMD is 1% to 2% (Moderate). ***Joint:*** Risk reduction of incident OA for various measures of walking ranges from 22% to 83% (Weak). Among adults with osteoarthritis, pooled effect sizes (ES) for pain relief are small to moderate (ES = 0.25 to 0.52); for function and disability ES are small (function ES = 0.14 to 0.49, disability ES = 0.32 to 0.46) (Strong). ***Muscular:*** The magnitude of the effect of resistance types of PA on muscle mass and function is highly variable and dose-dependent (Strong).
Is there any evidence for an effect of sex, age, race/ethnicity? (Strength of evidence in parentheses) ***Bone:*** There is evidence for a lower relative risk of hip fracture in older women and men; the evidence is more consistent in women (Moderate). Benefits of PA on BMD have been found to occur in premenopausal women, postmenopausal women, and adult men; the evidence is more consistent in women (Moderate). Information on race and ethnic specificity is lacking. ***Joint:*** Female sex and older age are established risk factors for incident OA (Strong), the evidence for race/ethnicity is equivocal (Weak). Male and female adults of any age with OA benefit from both aerobic and resistance exercise (Strong). Women may have a bigger benefit from resistance exercise, likely due to lower baseline muscular strength (Limited).

Health Outcome: Musculoskeletal Health (continued)

Muscular:

Benefits are similar in men and women and pervasive across the life span (Strong), although the magnitude of the benefits may be attenuated in old age (Moderate). Information on race and ethnic specificity is lacking.

Is there a dose-response effect? (Strength of evidence in parentheses)

Bone:

There is evidence of a dose-response association of PA with hip fracture risk (Moderate). Dose-response effects have not been adequately tested for PA and BMD.

Joint:

High-level (elite, professional) athletes competing in high joint-loading sports (e.g., football, soccer, track and field) may have an increased risk of hip/knee OA (Strong). Dose-response effects have not been tested with regard to PA among adults with arthritis.

Muscular:

There is a dose-response with greatest gains in muscle mass and muscle strength experienced with higher-intensity protocols (Strong).

What is an effective PA dose regarding mode, duration, intensity, and frequency that is supported by the evidence? (Strength of evidence in parentheses)

Bone:

PA of 4 or more hours per week of walking, 2 to 4 hours per week of LTPA, 9 to 14.9 MET hours per week of PA, and and1 hour per week of PA have been associated with a 36% to 41% lower risk in hip fracture risk. Weight-bearing endurance and resistance types of PA (i.e., exercise training) are effective in promoting increases in BMD (moderate-to-vigorous intensity; 3 to 5 days per week; 30 to 60 minutes per session). Walking-only protocols found a benefit on spine BMD (Moderate).

Joint:

For adults with arthritis, benefits in pain, function, and disability were noted with programs averaging a total volume of 130 to 150 minutes per week: 30 to 60 minutes per session; 3 to 5 days per week; moderate intensity; low-impact (Strong). Both aerobic and muscle strengthening activities improve joint function and reduce pain.

Muscular:

Progressive, high-intensity (60% to 80% of 1 repetition maximum [1RM]) muscle-strengthening activities can preserve or increase skeletal muscle mass, strength, power, and intrinsic neuromuscular activation (Strong).

Health Outcome: Musculoskeletal Health (continued)
What is the evidence on accumulation? (Strength of evidence in parentheses) ***Bone:*** The effects of accumulation have not been tested in humans. ***Joint:*** One study of fibromyalgia patients supports equal benefits (improved function, well-being, disease activity) for 2 15-minute sessions per day and 1 30-minute session per day of moderate-intensity, low-impact aerobic exercise (Limited). ***Muscular:*** The effects of accumulation have not been tested in humans.
What other unique comments should be made about the evidence of PA with this health outcome? ***Bone:*** Individual RCTs support basic science findings that intensity of loading forces is a key determinant of the skeletal response. Studies of laboratory animals also suggest that multiple, short bouts of PA should have more favorable effects on bone than a single, longer bout of PA. ***Joint:*** Joint injuries and excess body mass are more important risk factors for incident OA than sports/PA participation (Consistent, Strong). ***Muscular:*** Endurance types of PA do not increase muscle mass, but may attenuate the rate of loss with aging and preserve function (Moderate).

Health Outcome: Functional Health
Types of studies? ***Functional Health:*** Type 3a, Type 1 ***Falls:*** Type 1
What is the nature of the association of PA with Functional Health? (Strength of evidence in parentheses) ***Functional Health:*** There is observational evidence that mid-life and older adults who participate in regular PA have reduced risk of moderate/severe functional limitations and role limitations (Moderate to Strong). In older adults with existing functional limitations, there is fairly consistent evidence that regular PA is safe and has a beneficial effect on functional ability (Moderate); however, there is currently little or no experimental evidence in older adults with functional limitations that PA maintains role ability or prevents disability.

Health Outcome: Functional Health (continued)
Falls: In older adults at risk for falls, there is consistent evidence that regular PA is safe and reduces risk of falls (Strong).
What is the effect size? (Strength of evidence in parentheses) ***Functional Health:*** There is about a 30% risk reduction for the prevention or delay in function and/or role limitations with PA (Moderate to Strong). It is difficult to ascertain an effect size for the maintenance/improvements in functional ability due to the variety of outcomes measured. ***Falls:*** Older adults who participate in regular PA have about a 30% lower risk of falls (Strong).
Is there any evidence for an effect of sex, age, race/ethnicity? (Strength of evidence in parentheses) The association exists for both men and women with respect to preventing and maintaining or improving functional health and reducing risk of falls (Strong). The association exists for preventing functional limitations in middle-aged and older adults (Strong); the association for maintaining or improving functional heath is seen in older adults aged 65 years and older (Moderate); the association with falls reduction is seen in older adults at increased risk for falls (Strong). There is limited evidence to show an association exists for different race/ethnic groups for all outcomes (Weak).
Is there a dose-response effect? (Strength of evidence in parentheses) ***Functional Health:*** There appears to be a dose-response effect for PA in preventing or delaying function and/or role limitations, with greatest risk reduction seen with the highest levels of PA (Moderate). It is unclear whether there is a dose-response effect for PA in maintaining or improving functional ability, as this has not been tested. ***Falls:*** It is unclear whether there is a dose-response effect for PA in the reduction of falls in older adults, as this has not been tested.
What is an effective PA dose regarding mode, duration, intensity, and frequency that is supported by the evidence? (Strength of evidence in parentheses) ***Prevention:*** The most evidence of a dose response exists for walking activities (Strong); it is not possible at this point to ascertain dose of PA due to the nature of the study designs. ***Maintenance/Improvement:*** Evidence exists for exercise programs that include periods of 30 to 90 minutes of moderate-to-vigorous PA, 3 to 5 days per week, in which most of this time is devoted to aerobic and muscle-strengthening activities (with a smaller amount of time spent on other forms of activity, such as flexibility) (Moderate). When it was possible to determine the amount of time spent just on aerobic activity, studies usually varied from 60 minutes per week to 150 minutes per week (Moderate).

Health Outcome: Functional Health (continued)
Falls: Evidence exists for exercise programs that include 3 times per week of balance and moderate-intensity strengthening activities at 30 minutes per session, with additional encouragement to participate in moderate-intensity walking activities 2 or more times per week for 30 minutes a session (Strong).   Evidence also exists for tai chi exercises (Moderate). It was difficult to ascertain an optimal PA pattern for tai chi. Tai chi studies ranged from 1 hour per week to 3 hours or more per week (Limited).
What is the evidence around accumulation?   No evidence is available.
What other unique comments should be made about the evidence of PA with this health outcome?   Relative intensity is important to consider, as fitness levels are very low in many older adults.   It is important to increase exercise intensity and volume slowly to reduce adverse events, especially injuries.

Health Outcome: Cancer
Types of studies?   Type 3a – extensive
What is the nature of the association of PA with Cancer?   There is a clear inverse association between PA and prevention of breast and colon cancer.   Strength of evidence: Strong
What is the effect size?   There is about a 30% lower risk for colon cancer and about a 20% lower risk for breast cancer.   Strength of evidence: Strong
Is there any evidence for an effect of sex, age, race/ethnicity?   This association exists for both men and women for colon cancer, as well as for adults of different ages. There is reasonable evidence to show an association exists for different race/ethnic groups.   Strength of evidence: Sex = Strong, Age = Strong, Race/Ethnicity = Reasonable
Is there a dose-response effect?   There is a dose-response association between PA and the development of breast/colon cancer, but the shape of the curve is unclear.   Strength of evidence: Reasonable
What is an effective PA dose regarding mode, duration, intensity, and frequency that is supported by the evidence? (Strength of evidence in parentheses)   Data indicate at least 30 to 60 minutes per day of moderate-to-vigorous PA is needed to see significantly lower risks (Reasonable). Data are primarily for aerobic LTPA (Strong).

Health Outcome: Cancer (continued)
What is the evidence on accumulation? (Strength of evidence in parentheses) There is no information on accumulation of PA and cancer. However, the LTPA carried out by subjects in observational studies likely is accumulated from different activities of various, but unknown, duration (Limited).
What other unique comments should be made about the evidence of PA with this health outcome? (Strength of evidence in parentheses) There is a small body of Type 1 evidence for an association between improved quality of life and fitness in breast cancer survivors (Strong). There is growing evidence of a reduced risk of cancers of the endometrium and lung with increased physical activity (Reasonable).

Health Outcome: Mental Health
Types of studies? Type 1, 2a, 3a and 3b
What is the nature of the association of PA with Mental Health? There is clear evidence that PA reduces risk of depression and cognitive decline in adults and older adults. There is some evidence that PA improves sleep. There is limited evidence that PA reduces distress/well-being and anxiety. Strength of evidence: Depression and cognitive health = Strong; Sleep = Moderate; Distress/well-being and Anxiety = Limited
What is the effect size? There is about a 20% to 30% lower risk for depression, distress/well-being, and dementia. Strength of evidence: Strong
Is there any evidence for an effect of sex, age, race/ethnicity? Risk reduction has been observed for men and women of all ages, but few studies have directly compared results according to sex or age. Racial/ethnic minority groups have been underrepresented in most studies, but limited results from prospective cohort studies suggest that risk reduction among blacks and Hispanic/Latinos is similar to that among whites. Strength of evidence: Limited
Is there a dose-response effect? (Strength of evidence in parentheses) Reasonable evidence indicates a dose-response effect between PA and mental health. Moderate and high levels of physical activity are similarly associated with lower risk of depression and distress/well-being, compared to low levels of physical activity exposure, which is nonetheless more protective than inactivity or very low levels of physical activity (Moderate). There is insufficient evidence to determine whether there are dose-response relations with physical activity for anxiety, cognitive health, and sleep (Limited).

Health Outcome: Mental Health (continued)
What is an effective PA dose regarding mode, duration, intensity, and frequency that is supported by the evidence? Most evidence comes from PA programs of 3 to 5 days per week, 30 to 60 minutes per session and moderate to vigorous intensity. Most evidence comes from aerobic and multi-modal interventions (usually aerobic plus muscle strengthening activities). Only a few studies have manipulated and compared features of physical activity and their effects on mental health. Aerobic or resistance, and their combination, have positive effects. However, the minimal or optimal type or amount of exercise for mental health is not yet known Strength of evidence: Limited to Moderate
What is the evidence on accumulation? Mental health outcomes have not differed when physical activity was continuous or intermittent in nature, but studies have not directly compared single versus multiple sessions of similar amounts of physical activity in controlled studies. Hence, there is insufficient evidence to determine whether physical activity can be accumulated to achieve mental health benefits. Strength of evidence: Limited
What other unique comments should be made about the evidence of PA with this health outcome? Positive findings from initial studies suggest that physical activity and exercise might reduce the onset, progression, or adverse impact of central nervous system disorders other than dementia that contribute to disability and mortality risk, such as multiple sclerosis and Parkinson's disease. Benefits of physical activity may also extend to other aspects of mental health that are important contributors to overall quality of life, such as self-esteem and feelings of energy/fatigue. Sufficient evidence exists to encourage more study in these areas, but presently not enough studies are available to draw conclusions about how the effects of physical activity or exercise may differ according to types of people or types and amounts of physical activity.

Health Outcome: Youth
Types of studies? ***Physical Fitness***: Type 1, 2a, 2b, 3a, 3b: Cardiorespiratory Type 2b: Muscular Strength ***Body Mass and Composition***: Type 1, 2b, 3a, 3b ***Cardiovascular and Metabolic Health***: Type 1, 2b, 3a, 3b ***Bone Health***: Type 1, 3a ***Mental Health:*** Type 1, 2b, 3a, 3b: Depression Type 1, 3b: Anxiety

Health Outcome: Youth (continued)
What is the nature of the association of PA with health for Youth? (Strength of evidence in parentheses) ***Physical Fitness***: There is a clear, positive association between PA and cardiorespiratory fitness and muscular strength (Strong). ***Body Composition***: There is a clear, positive association between PA and favorable body composition (Strong). ***Cardiovascular and Metabolic Health***: There is a clear, positive association between PA and cardiovascular and metabolic health (Strong). ***Bone Health***: There is a clear, positive association between PA and bone health (Strong). ***Mental Health:*** There appears to be an association between PA and reduced symptoms of depression (Moderate), anxiety (Weak), and higher self esteem (Limited).
Is there a dose-response effect? ***Cardiovascular and Metabolic Health***: There appears to be a dose-response relationship; however, the precise pattern of this relationship has not been determined. ***Other Outcomes***: Either evidence is insufficient or the varying methodologies and insufficient numbers of intervention trials preclude inferences about dose-response patterns for the remainder of the outcomes. Dose-response studies are needed.
Is there any evidence for an effect of sex, age, race/ethnicity? (Strength of evidence in parentheses) ***Physical Fitness***: The association between PA and cardiorespiratory fitness and muscle strength exists for both boys and girls, as well as in children and adolescents (Strong). The research is not adequate to draw conclusions about race/ethnicity. ***Body Composition***: The research is not adequate to draw conclusions about age, biological maturity, and race/ethnicity for body mass and composition. ***Cardiovascular and Metabolic Health***: Very little is known about the effects of sex, age, biological maturity, and race/ethnicity on the relationship of PA to cardiovascular and metabolic health.

Health Outcome: Youth (continued)
Bone Health: This association exists for both boys and girls, and is influenced by age and developmental status (Strong). The window of opportunity appears to be in puberty and pre-menarchal years (Moderate). The research is not adequate to draw conclusions about race/ethnicity. ***Mental Health***: The research is not adequate to draw conclusions about sex, age, maturity, and race/ethnicity on the relationship of PA to mental health.
What is an effective PA dose regarding mode, duration, intensity, and frequency that is supported by the evidence? ***Overall Conclusion***: Important health and fitness benefits can be expected by most children and youth who participate daily in 60 or more minutes of moderate-to-vigorous physical activity (Strong). ***Physical Fitness***: Vigorous aerobic activity 3 or more days per week significantly improves cardiorespiratory fitness. Resistance training 2 or 3 days per week significantly improves muscular strength. ***Body Composition***: Reductions in overall adiposity and visceral adiposity with exposure to regular moderate-to-vigorous PA 3 to 5 days per week for 30 to 60 minutes have been observed. ***Cardiovascular and Metabolic Health:*** Vigorous aerobic activity 3 or more days per week significantly improves cardiovascular and metabolic health. ***Bone Health***: Targeted weight-loading activities that simultaneously influence muscular strength, done 3 or more days per week, significantly improve bone mineral content and density.
What other unique comments should be made about the evidence of PA with this health outcome? ***Overall Conclusions***: It is important to minimize the potential risks of overtraining and injuries. A wide-range of developmentally appropriate activities for children should be chosen.

Health Outcome: Understudied Populations
Types of studies? Type 1, 2a, 2b
What is the nature of the association of PA with health for people with disabilities? Consistency of evidence supports the use of PA to improve key health outcomes in people with physical and cognitive disabilities. Strength of evidence: ***Physical Disability***: The strongest evidence is found under the categories of cardiorespiratory, musculoskeletal, and mental health. ***Cognitive Disability***: The strongest evidence is found under the categories of functional health and mental health.
What is the effect size? N/A Level of evidence was based on number of significant trials reporting positive outcomes. Definition of strength of evidence: ***Strong***: At least 75% of reviewed trials significant. ***Moderate***: 50% to 74% of reviewed trials significant. ***Limited***: Up to 49% of reviewed trials significant. Strength of evidence: ***Physical Disability***: Strong for cardiorespiratory health, musculoskeletal health, and mental health; Moderate for functional health. ***Cognitive Disability***: Strong for functional health and mental health; Moderate for cardiorespiratory health, musculoskeletal health, and healthy weight and metabolic health.
Is there any evidence for an effect of sex, age, race/ethnicity? No
Is there a dose-response effect? No direct data on dose response are available.
What is an effective PA dose regarding mode, duration, intensity, and frequency that is supported by the evidence? (Strength of evidence in parentheses) The majority of the studies included exercise doses typically used in studies with the general population: Intensity: 50% or more of heart rate reserve or VO_{2peak} (Strong) Frequency: 3 to 5 days per week (Strong) Duration: 30 to 60 minutes (Strong)

Health Outcome: Understudied Populations (continued)
What is the evidence on accumulation? No direct data are available on multiple bouts versus one long bout.
What other unique comments should be made about the evidence of PA for people with disabilities? PA is relatively safe and effective for people with disabilities and can improve several key health outcomes. Very few serious adverse events have been reported (1.15% exercise versus 0.60% for controls).

Health Outcome: Adverse Events
Types of studies? Types: 1, 3a, 4
What is the nature of the association of PA with Adverse Events? (Strength of evidence in parentheses) The risk of musculoskeletal injuries is lower for non-contact (e.g., walking) and limited contact (e.g., baseball) activities than for contact (e.g., basketball) and collision (e.g., football) activities (Strong). The usual dose of regular physical activity is directly related to the risk of musculoskeletal injury (Strong) and inversely related to the risk of sudden adverse cardiac events (Strong). The risk of musculoskeletal injuries and sudden cardiac adverse events is directly related to the size of the difference between the usual dose of activity and the new or momentary dose of activity (Strong). The most consistently reported risk factor for musculoskeletal injuries (Strong) and sudden cardiac adverse events (Strong) is inactivity and low fitness.
Is there any evidence for an effect of sex, age, race/ethnicity? Older people are more susceptible to activity-related musculoskeletal injuries (Weak). Females are more likely than males to suffer musculoskeletal injuries, but the difference appears to be due to lower fitness (Weak). Differences in the risk of musculoskeletal injuries among different race/ethnicity groups do not appear to be marked but have been infrequently studied (Weak).
What is an effective PA dose regarding mode, duration, intensity, and frequency that is supported by the evidence? A series of small increases in activity each followed by a period of adaptation will cause fewer adverse events than will larger or more frequent increases in activity (Weak). The incidence of adverse events caused by moderate-intensity physical activity appears to be low (Weak).

Health Outcome: Adverse Events (continued)
What other unique comments should be made about the evidence of PA and Adverse Events? The benefits of regular physical activity far outweigh the risks of adverse events for outcomes that encompass a broad spectrum of medical maladies such as all-cause mortality (Strong), functional health (Moderate), and medical expenditures (Strong). Appropriate clothing, gear, and equipment, as well as a safe environment, reduce the risk of adverse events.

Integrating the Evidence: Questions and Answers About the Health Benefits of Physical Activity

After it summarized the evidence linking physical activity to a variety of health outcomes and populations, the PAGAC's next step was to integrate this evidence in the following questions and responses. Because the primary charge to the PAGAC was to review the scientific evidence to inform the development of public health physical activity guidelines and policy for Americans, the questions and answers primarily focus on major outcomes and on issues involving dose response, particularly the minimum amount, intensity, duration, and frequency associated with health benefits, as well as whether additional health benefits are observed at higher levels of physical activity.

Overall Benefits of Physical Activity

Q-1. *Does existing evidence indicate that people who are habitually physically active have better health and a lower risk of developing a variety of chronic diseases than do inactive people?*

R-1. Yes. Very strong scientific evidence based on a wide range of well-conducted studies shows that physically active people have higher levels of health-related fitness and a lower risk profile for developing a number of disabling medical conditions than do people who are inactive. In **children and youth** major benefits supported by strong evidence include enhanced cardiorespiratory and muscular fitness, cardiovascular and metabolic health biomarkers, bone health, body mass and composition. Less strong evidence supports selected measures of mental health. In **adults and older adults** strong evidence demonstrates that, compared to less active counterparts, more active men and women have lower rates of all-cause mortality, coronary heart disease, high blood pressure, stroke, type 2 diabetes, metabolic syndrome, colon cancer, breast cancer, and depression. Strong evidence also supports the conclusion that, compared to less active people, physically active adults and older adults exhibit a higher level of cardiorespiratory and muscular fitness, have a healthier body mass and composition, and a biomarker profile that is more favorable for the preventing cardiovascular disease and type 2 diabetes and enhancing bone health. Modest evidence indicates that physically active adults and older adults have better quality sleep and health-related quality of life. For **older adults**, strong evidence indicates that being physically active is associated with higher levels of functional health, a lower risk of falling, and better cognitive function.

Time course for benefits. Strong evidence indicates that increases in cardiorespiratory and muscular fitness and improvements in various biomarkers that appear in the causal pathways between increased activity and favorable clinical outcomes and in some clinical outcomes, such as a decrease in depression, frequently occur in weeks or a few months in response to a sustained increase in moderate- to vigorous-intensity activity. The time course for a decrease in occurrence of various chronic disease clinical outcomes has not been established but appears to require longer exposure to an increased level of activity.

Q-2. What does the evidence indicate about dose of physical activity that is most likely to provide many of the benefits indicated in R-1?

R-2. Current science, inter-individual differences in the biological responses to specific activity regimens and the wide variety of benefits provided by being physically active do not allow a single, highly precise answer to this question. However, as a starting place for overall public health benefit, data from a large number of studies evaluating a wide variety of benefits in diverse populations generally support 30 to 60 minutes per day of moderate- to vigorous-intensity physical activity on 5 or more days of the week. For a number of benefits, such as lower risk for all-cause mortality, coronary heart disease, stroke, hypertension, and type 2 diabetes in adults and older adults, lower risk is consistently observed at 2.5 hours per week (equivalent to 30 minutes per day, 5 days per week) of moderate- to vigorous-intensity activity. The amount of moderate- to vigorous-intensity activity most consistently associated with significantly lower rates of colon and breast cancer and the prevention of unhealthy weight gain or significant weight loss by physical activity alone is in the range of 3 to 5 hours per week.

By converting the intensity and duration of various aerobic activities into MET-minutes or MET-hours (intensity in METs x duration), it is possible to combine activities of different types and intensities into a single measure of amount of activity. For many studies, the amount of moderate- and vigorous-intensity activity associated with significantly lower rates of disease or improvements in biomarkers and fitness is in the range of 500 to 1,000 MET-minutes per week. An adult can achieve a target of 500 MET-minutes per week by walking at about 3.0 miles per hour for approximately 150 minutes per week (7.5 miles), walking faster at 4.0 miles per hour for 100 minutes (6.6 miles) or jogging or running at 6 miles per hour for about 50 minutes per week (5.0 miles). To achieve 1,000 MET-minutes per week, these amounts of activity would need to be doubled. These MET-minutes per week targets also can be achieved by performing various combinations of activities of different intensities and durations (See Table D.3 in ***Part D: Background*** and its accompanying text for more details).

Very limited data are available on dose response in children and youth, but strong evidence indicates that better fitness and health outcomes are observed when 60 minutes of moderate- to vigorous-intensities activity of various types is accumulated throughout the day.

Q-3. *Is there evidence that performing more than 30 minutes per day of moderate- to vigorous-intensity activity on most days confers greater health benefits for some health outcomes?*

R-3. Yes. For a variety of health and fitness outcomes, including chronic disease prevention, improvement of various disease biomarkers and the maintenance of a healthy weight, reasonably strong evidence demonstrates that amounts of moderate- to vigorous-intensity activity that exceed 150 minutes per week are associated with greater health benefits. However, in a number of studies where such a dose response is observed in preventing chronic disease or reducting all-cause mortality, the relation appears to be curvilinear. This means that the absolute increase in benefits becomes less and less for any given increase in the amount of physical activity. An example of a curvilinear dose-response relation between the relative risk of all-cause mortality and the amount of moderate-to-vigorous physical activity in hours per week is displayed in Figure G1.3 (***Part G. Section 1: All-Cause Mortality).*** As stated in that chapter, "On average, compared to less than 0.5 hours per week of moderate-to-vigorous physical activity, engaging in approximately 1.5 hours per week in such activity is associated with about a 20% reduction in risk of all-cause mortality during follow-up. Additional amounts of physical activity are associated with additional reductions, but at smaller magnitudes, such that approximately 5.5 hours per week is required to observe a further 20% reduction in risk (i.e., approximately 7.0 hours per week is associated with approximately 40% reduction in risk compared with less than 0.5 hours per week)." A somewhat similar curvilinear relation appears to exist between amounts of moderate to vigorous activity and risk of coronary heart disease. The added value of higher amounts of activity for helping maintain a healthy body weight is discussed in the responses to Questions 15 to 17.

Q-4. *For people who are physically inactive or unfit, does current science support the concept that some activity is better than none?*

R-4. PAGAC members spent substantial time considering this question and concluded that for otherwise healthy sedentary individuals, some physical activity is better than none. The least active in the population generally have the highest risk for various negative health consequences and the most to gain from becoming more active. Increasing evidence suggests that performing activity in amounts of no more than about 1 hour per week at an intensity that is moderate relative to the person's capacity will provide small increases in cardiorespiratory and muscular fitness. In some studies, this amount of activity is associated with lower risk of all-cause mortality and the incidence of coronary heart disease. At this lower amount and intensity of activity, the benefits usually are less than that observed with greater amounts of activity, and studies are much less consistent about the nature and magnitude of these benefits. Nevertheless, the dose-response curves for the major health benefits clearly indicate an inverse relation between the dose of activity and rate of disease. Although the minimum amount of activity needed to produce a benefit cannot be stated with certainty, nothing would suggest a threshold below which there are no benefits. Therefore, for inactive adults any increase appears better than none. To achieve benefits for various health outcomes equivalent to those achieved by their more active peers, very inactive adults will need to progress gradually to higher amounts and intensities of activity.

Q-5. If physical activity is performed at a vigorous intensity, are the health outcomes greater than what has been observed with moderate-intensity activity?

R-5. Yes. For some favorable health and fitness outcomes strong evidence indicates that an increase in intensity is associated with greater improvements compared to those observed with moderate-intensity activity. For example, when a similar amount of activity is performed per session, such as walking 3 miles per day, participants who walk faster have a greater increase in cardiorespirtaory fitness than those who walk more slowly. One problem in interpreting data that compares the benefits of moderate versus vigorous activity in many observational and experimental studies is that along with a difference in intensity between study groups, the amount or volume of activity performed also differs. For example, if participants in two groups are physically active 30 minutes per day 5 days per week, but one group walks at 3 miles per hour and the other jogs at 6 miles per hour, both the intensity and the amount of activity performed will be different between the two groups. In this case it is not possible to tell for sure whether differences in health or fitness outcomes between the 2 groups are due to the difference in the intensity or the amount of activity performed, or both. It is important to recognize that the rate of energy expenditure goes up quite rapidly with increases in intensity for some types of activity, such as going from walking to jogging or running.

As people consider increasing their physical activity to high doses of vigorous-intensity activity with the primary goal of achieving favorable health outcomes, they need to be aware that such increases may accelerate the injury rate disproportionate to the benefits accrued. This appears to be especially true for people who have been inactive for extended periods and who then rapidly increase the amount and/or intensity of activity they perform.

Q-6. Is there evidence that the frequency of physical activity sessions influences health and fitness outcomes independent of the amount of activity performed?

R-6. Very limited published research has systematically evaluated health or fitness benefits in response to different frequencies of activity sessions per week when the amount of activity is held reasonably constant. In experimental studies, comparisons have been made between 2 versus 3 or more sessions per week for both aerobic and resistance activity, but the amount of activity performed increased as the number of sessions increased so it is not possible to separate out the effects of increasing the session frequency from the effects of increasing the amount. Most of the data from prospective cohort studies with outcomes of all-cause mortality or chronic disease morbidity and mortality do not provide information about frequency of activity independent of intensity and amount, but the very limited data available indicate that when activity amount is controlled for, the effect of session frequency is not significant.

When many adults with sedentary occupations reach the range of 500 to 1,000 MET-minutes per week of leisure-time physical activity (LTPA), it is very likely that this activity is the result of multiple sessions performed during the week. Experimental studies that show significant improvements in health-related outcomes typically feature session frequencies ranging between 3 and 5 times per week. Also, as the response to the Question 7 demonstrates, a growing, but still limited, body of evidence indicates that multiple short bouts (10 or more minutes) per day of aerobic activity produces improvements in cardiorespiratory fitness and selected cardiovascular disease (CVD) biomarkers similar to that obtained with a single bout of equal total duration and intensity.

Overall, one interpretation of the existing data is that for health and fitness benefits, the frequency of activity is much less important than the amount or intensity. Many experimental studies since 1995 have demonstrated beneficial effects of 120 to 150 minutes per week of moderate- or vigorous-intensity activity usually performed during 3 to 5 sessions per week, so we know that this frequency of activity is effective. Only limited data are available comparing the benefits from just one or two sessions per week with multiple sessions spread throughout the week with activity amount and intensity held constant. Again, while very limited data are available from direct comparisons, the rate of certain types of adverse events (e.g., joint irritation, muscle soreness) may be lower when performing a similar amount and intensity of activity but during more sessions per week.

Q-7. Is there evidence that physical activity can be accumulated throughout the day for some health and fitness outcomes?

R-7. The concept of accumulation refers to performing multiple short bouts of physical activity throughout the day. Some scientific evidence of moderate strength suggests that accumulating 30 or more minutes per day of moderate- to vigorous-intensity aerobic activity throughout the day in bouts of 10 minutes or longer produces improvements in cardiorespiratory fitness. Limited data indicate that accumulated short bouts improve selected CVD biomarkers in a manner generally similar to that observed when activity of a similar amount and intensity is performed in a single bout of 30 or more minutes. These experimental studies have primarily evaluated the effects of multiple short bouts of 8 to 10 minutes duration versus longer bouts of 30 to 40 minutes and have not provided data on numerous shorter bouts (e.g., 30 1-minute bouts per day). Data on the effects of accumulating activity involving multiple short bouts for the prevention of major clinical outcomes, such as all-cause mortality, CVD, diabetes, and selected cancers, are very limited because of the type of data collected from questionnaires used in most prospective observational studies. Using data from these questionnaires, it has not been possible to precisely differentiate between activities conducted in a single, long bout versus those conducted in multiple, short bouts over the day. Prospective cohort studies with clinical outcomes have tended to present their data according to categories of the total amount of activity performed, and this total amount is likely to be accumulated from different activities of varying, but unknown durations and frequencies, over the course of the day.

Q-8. Is there evidence that performing bouts of walking as a frequent routine is associated with positive health effects?

R-8. Yes. Strong evidence shows that a regimen of brisk walking provides a number of health and fitness benefits for adults and older adults. For example, women in the United States who walk 2 to 3 hours per week have a significantly lower risk of all-cause mortality and cardiovascular disease than do women who report no or very little walking. Also, for people walking for equivalent amounts of time, a faster pace is associated with a lower risk of cardiovascular disease, type 2 diabetes, and all-cause mortality. Strong evidence also shows that frequent bouts of walking increase cardiorespiratory fitness, especially in people who have been performing little activity on a regular basis. Limited to moderate evidence suggests that walking helps to maintain bone density and reduce fractures over time, especially in women, and helps to maintain joint health and functional ability in adults and older adults.

Q-9. What does the scientific evidence indicate about the pattern of physical activity that is most likely to produce the fewest adverse medical events while providing health benefits?

R-9. Much of the research that addresses this question has evaluated the risk of musculoskeletal injuries or sudden cardiac death during vigorous physical activity (e.g., jogging, running, competitive sports, military training) with few well-conducted studies evaluating the risk during moderate-intensity activity intended primarily to improve health. Activities with fewer and less forceful contact with other people or objects have appreciably lower injury rates than do collision or contact sports. Walking for exercise, gardening or yard work, bicycling or exercise cycling, dancing, swimming, and golf, which are already popular in the United States, are activities with the lowest injury rates. Risk of musculoskeletal injury during activity increases with the total volume of activity (e.g., MET-hours per week). Intensity, frequency, and duration of activity all contribute to the risk of musculoskeletal injuries but their relative contributions are unknown. For sudden cardiac adverse events, intensity appears to be more important than frequency or duration. The limited data that do exist for medical risks during moderate-intensity activity indicate that the risks are very low for activities like walking and that the health benefits from such activity outweigh the risk.

Q-10. What does the scientific evidence say about actions that can be taken to reduce the risk of injury during physical activity?

R-10. Research with a variety of populations and methods indicates that injuries are more likely when people are more physically active than usual. The key point to remember, however, is that when individuals do more activity than usual, the risk of injury is related to the size of the increase. A series of small increments in physical activity each followed by a period of adaptation is associated with lower rates of musculoskeletal injuries than is an abrupt increase to the same final level. Although the safest method of increasing one's physical activity has not been empirically established, adding a small and comfortable amount of light to moderate-intensity activity such as walking, 5 to 15 minutes per session, 2 to 3 times per week, has a low risk of musculoskeletal injury and no known risk of sudden severe cardiac events.

For people with stable activity habits, risk of injury is directly related to the total volume of activity performed. Other things being equal, people who are very physically active are more likely to incur an activity-related injury than people who are active to a lesser degree. Some evidence suggests, however, that even though more active people are more likely to incur a physical activity-related injury they may suffer fewer overall injuries because they are less likely to be injured in other settings such as at work or around the home.

Q-11. Is there evidence regarding who should see a physician or have a medical examination before increasing the amount or intensity of physical activity they perform?

R-11. The protective value of a medical consultation for persons with or without chronic diseases who are interested in increasing their physical activity level is not established. No evidence is available to indicate that people who consult with their medical provider receive more benefits and suffer fewer adverse events than people who do not. Also unknown is the extent to which official recommendations to seek medical advice before augmenting one's regular physical activity practices may reduce participation in regular moderate physical activity by implying that being active may be less safe and provide fewer benefits than being inactive.

Q-12. What are the major health benefits provided by an increase in aerobic (endurance) activity?

R-12. Aerobic activity of moderate to vigorous intensity performed on a regular basis results in improvements in cardiorespiratory fitness (VO_{2max}) with an increase in the capacity and efficiency of the cardiorespiratory system to transport oxygen to skeletal muscles and for muscles to use this oxygen. This increase in cardiorespiratory fitness has a strong inverse association with risk of all-cause mortality and a variety of chronic diseases. The evidence is strong that aerobic activity has favorable effects on various biomarkers for CVD and type 2 diabetes (e.g., atherogenic lipoprotein profile, blood pressure, insulin sensitivity) in adults and older adults with and without these diseases. Much of the physical activity associated with lower risk for all-cause mortality, coronary heart disease, stroke, hypertension, breast and colon cancer, and depression in many of the prospective observational studies published since 1995 has been moderate- to vigorous-intensity aerobic activity. For most people, performing aerobic activity that requires the rhythmic use of large muscles and the movement of the body mass against gravity (e.g., walking, jogging, cycling, climbing stairs, dancing) is the most effective way to increase the rate of energy expenditure and better achieve energy balance. For many of the benefits linked to preventing various chronic diseases, aerobic activity performed at moderate to vigorous intensity in the range of 500 to 1,000 MET-minutes per week is associated with a significantly lower risk.

Q-13. What are the major health benefits provided by resistance or muscle-strengthening activity?

R-13. Strong evidence exists in youth, adults and older adults that muscle-strengthening exercises that load skeletal muscle and bone increase muscle mass, strength, and quality and increase bone mineral density. Evidence is moderate that muscle-strengthening exercises improve functional ability in older adults and lead to improvements in muscle strength, joint pain, stiffness, and functional ability in adults with osteoarthritis. In combination with balance training, muscle-strengthening exercises reduce risk of falls in older adults at risk for falls (this evidence is discussed in more detail in Question 22). Resistance exercise can help maintain lean body mass during a program of weight loss, but by itself results in little weight loss.

Most of the evidence supports a resistance activity program with the following characteristics: progressive muscle strengthening exercises that target all major muscle groups performed on 2 or more days per week. To enhance muscle strength, 8 to 12 repetitions of each exercise should be performed to volitional fatigue. One set is effective; however, limited evidence suggests that 2 or 3 sets may be more effective.

Q-14. What is the evidence that flexibility activities provide health benefits?

R-14. Flexibility is an important element of overall fitness. However, the evidence that flexibility exercises by themselves confer health benefits is very limited. Most well-designed exercise interventions in youth, adults, and older adults include a brief flexibility routine as part of the intervention and often as the control condition, thus preventing the assessment of the relative benefits of flexibility training alone. Some evidence indicates that balanced exercise interventions that include flexibility activities reduce the risk of injuries.

Energy Balance

Q-15. What is the amount of physical activity that is necessary for weight stability over the long term?

R-15. The optimal amount of physical activity needed for weight maintenance (defined as less than 3% change in weight) over the long-term is unclear. However, the evidence is clear that physical activity provides benefit for weight stability. A great deal of inter-individual variability exists with physical activity and weight stability, and many persons may need more than 150 minutes of moderate-intensity activity per week to maintain weight. Data from recent well-designed randomized controlled trials lasting up to 12 months indicate that aerobic physical activity performed to achieve a volume of 13 to 26 MET-hours per week is associated with approximately a 1% to 3% weight loss (i.e., an amount generally considered to represent weight stability). Thirteen MET-hours per week is approximately equivalent to walking at 4 miles per hour for 150 minutes per week or jogging at 6 miles per hour for 75 minutes per week.

Q-16. What is the evidence for the amount of physical activity that is necessary for weight loss in adults?

R-16. A wide range of studies provides evidence of a dose-response relation between physical activity and weight loss. Clear, consistent data show that a large volume of physical activity is needed for weight loss in the absence of concurrent dietary changes. The physical activity equivalent of 26 kilocalories per kilogram of body weight (1,560 MET-minutes) or more per week is needed for weight loss of 5% or greater. Smaller amounts of weight loss are seen with smaller amounts of physical activity (as noted in R-15). This relatively high volume of physical activity is equivalent to walking about 45 minutes per day at 4 miles per hour or about 70 minutes per day at 3 miles per hour, or jogging 22 minutes per day at 6 miles per hour.

The role of energy intake (diet) must be considered in any discussion of weight control. When calorie intake is carefully controlled at a baseline level, the magnitude of any weight loss is what would be expected given the increase in energy expenditure of the person's physical activity. However, in situations in which people's dietary intake is not controlled, the amount of weight loss due to the increase in physical activity is not commensurate to what would be expected. Therefore, for most people to achieve substantial weight loss (i.e., more than 5% decrease in body weight), a dietary intervention also is needed. The dietary intervention could include either maintenance of baseline caloric intake, or a reduction in caloric intake to accompany the physical activity intervention. The magnitude of change in weight due to physical activity is additive to that associated with caloric restriction.

Q-17. Is there evidence that physical activity provides benefit for weight maintenance in adults who have previously lost substantial body weight?

R-17. The scientific evidence for the effectiveness of physical activity alone in preventing weight regain following significant weight loss is limited. Available data indicate that to prevent substantial weight regain over 6 months or longer, many adults need to exercise in the range of 60 minutes of walking or 30 minutes of jogging daily (approximately 4.4 kilocalories per kilogram per day of activity energy expenditure). The literature generally supports the concept that "more is better" for long-term weight maintenance following weight loss. Further, the evidence indicates that individuals who are successful at long-term weight maintenance appear to limit caloric intake in addition to maintaining physical activity.

Q-18. For people who are overweight or obese is there evidence that physical activity provides health benefits irrespective of assisting with energy balance?

R-18. Yes. Strong evidence shows that physically active adults who are overweight or obese experience a variety of health benefits that are generally similar to those observed in people of optimal body weight (BMI = 18.5-24.9). These benefits include lower rates of all-cause mortality, coronary heart disease, hypertension, stroke, type 2 diabetes, colon cancer, and breast cancer. At least some of these benefits appear to be independent of a loss in body weight, while in some cases weight loss in conjunction with an increase in physical activity results in even greater benefits. Because of the health benefits of physical activity that are independent of body weight classification, adults of all sizes and shapes gain health and fitness benefits by being habitually physically active.

Youth

Q-19. What does the evidence indicate about the major physical fitness and health benefits of physical activity in children and youth?

R-19. Strong evidence demonstrates that the physical fitness and health status of children and youth is substantially enhanced by frequent physical activity. Compared to inactive young people, physically active children and youth have higher levels of cardiorespiratory endurance and muscular strength and well documented health benefits include lower body fatness, more favorable cardiovascular and metabolic disease risk profiles, enhanced bone health, and reduced symptoms of anxiety and depression. These conclusions are based on the results of observational studies in which higher levels of physical activity were found to be associated with favorable health parameters as well as experimental studies in which exercise treatments caused improvements in physical fitness and various health-related factors.

Q-20. What does the evidence indicate about the dose of physical activity that is most likely to provide health benefits for children and youth?

R-20. Few studies have provided data on the dose response for various health and fitness outcomes in children and youth. However, substantial data indicate that important health and fitness benefits can be expected to accrue to most children and youth who participate daily in 60 or more minutes of moderate to vigorous physical activity. Also, the Committee concluded that certain specific types of physical activity should be included in an overall physical activity pattern in order for children and youth to gain comprehensive health benefits. These include regular participation in each of the following types of physical activity on 3 or more days per week: resistance exercise to enhance muscular strength in the large muscle groups of the trunk and limbs, vigorous aerobic exercise to improve cardiorespiratory fitness and cardiovascular and metabolic disease risk factors, and weight-loading activities to promote bone health.

Older Adults

Q-21. Is there evidence that the target dose for physical activity should differ for older adults?

R-21. Yes. If a person has a low exercise capacity (physical fitness), the intensity and amount of activity needed to achieve many health-related and fitness benefits is less than for someone who has a higher level of activity and fitness. For example, relative improvements in cardiorespiratory endurance and muscle strength produced by an increase in physical activity are more closely associated with the activity intensity relative to the capacity of the individual (e.g., percent of VO_{2max} or one repetition max [1RM]) than to the absolute intensity of the activity (e.g., 6 miles per hour or 100 pounds). Because the exercise capacity of adults tends to decrease as they age, older adults generally have lower exercise capacities than younger persons. Thus, they need a physical activity plan that is of lower absolute intensity and amount (but similar in relative intensity and amount) than is appropriate for more fit people, especially when they have been sedentary and are starting an activity program.

Q-22. What is the evidence that physical activity in older adults can reduce or prevent falls?

R-22. For older adults at risk of falling, strong evidence exists that regular physical activity is safe and reduces falls by about 30%. Most evidence supports a program of exercise with the following characteristics: 3 times per week of balance training and moderate-intensity muscle-strengthening activities for 30 minutes per session and with additional encouragement to participate in moderate-intensity walking activities 2 or more times per week for 30 minutes per session. Some evidence, albeit less consistent, suggests that tai chi exercises also reduces falls. Successful reduction in falls by tai chi interventions resulted from programs conducted from 1 to 3 hours or more per week. No evidence indicates that planned physical activity reduces falls in adults and older adults who are not at risk for falls.

Understudied Populations

Q-23. Is there evidence that physical activity provides health benefits to persons with various disabilities?

R-23. Yes. However, for many physical and cognitive disabilities, scientific evidence for various health and fitness outcomes is still limited due to the lack of research. The goal of the scientific review in persons with disabilities was not to consider exercise as a therapy for disability but to evaluate the evidence that physical activity provides the general health and fitness benefits frequently reported in populations without these disabilities (e.g., improvements in physical fitness, biomarkers for chronic disease, physical independence, health-related quality of life). Moderate to strong evidence indicates that increases in aerobic exercise improve cardiorespiratory fitness in individuals with lower limb loss, multiple sclerosis, stroke, spinal cord injury, and mental illness. Limited data show similar results for people with cerebral palsy, muscular dystrophy, and Alzheimer's disease. Moderate to strong evidence also exists for improvements in walking speed and walking distance in patients with stroke, multiple sclerosis, and intellectual disabilities. Quite strong evidence indicates that resistance exercise training improves muscular strength in persons with such conditions as stroke, multiple sclerosis, cerebral palsy, spinal cord injury, and intellectual disability. Although evidence of benefit is suggestive for such outcomes as flexibility, atherogenic lipids, bone mineral density, and quality of life, the data are still very limited.

For a majority of the studies reviewed involving persons with disabilities, the exercise regimen followed was that currently recommended for the general public — aerobic exercise of 30 to 60 minutes, 3 to 5 days per week at moderate intensity, and resistance training with 1 or 2 sets of 8 to 12 repetitions using appropriate muscle groups 2 to 3 times per week (intensity adjusted for the individual's capacity). Data comparing various doses of exercise in a single study are not available. In the studies reviewed, participants had to meet study eligibility and, in some cases, had to have a pre-participation medical evaluation, but the medical adverse event rate was low and did not differ between exercise program participants and non-exercise controls.

Q-24. Is there evidence regarding the health benefits as well as risks of physical activity for women during pregnancy and the postpartum period?

R-24. Substantial data from observational studies indicates that moderate-intensity physical activity by generally healthy women during pregnancy increases cardiorespiratory fitness without increasing the risk of low birth weight, preterm delivery, or early pregnancy loss. The results of several studies also indicate that moderate-intensity physical activity does not increase the risk of preeclampsia. Available data from recent observational studies show a favorable association between moderate-intensity activity during early pregnancy and somewhat lower rates of preeclampsia and gestational diabetes mellitus (GDM), although these data are not yet conclusive. For moderate-intensity activity during pregnancy, the scientific evidence is strong that the risks are very low, but the science is less strong in documenting improved health outcomes for the mother or child. The few studies that have been conducted on the risks and benefits of vigorous activity by women who are pregnant provide very limited data that this level of activity is associated with small reductions in birth weight compared to birth weights of infants born to less active women.

Moderate-intensity physical activity during the postpartum period does not appear to adversely affect milk volume or composition or infant growth, and moderately strong evidence suggests that it results in enhanced cardiorespiratory fitness and mood of the mother. Physical activity alone does not produce weight loss except when combined with dietary changes.

Dose-response studies of physical activity and health outcomes for moderate- or vigorous-intensity physical activity during pregnancy or the postpartum period have not been conducted. Most studies evaluating possible benefits have promoted moderate-intensity activity for 120 to 150 minutes per week.

Q-25. Is there evidence that the physical activity dose for improving health and fitness should differ for people depending upon race or ethnicity?

R-25. Since 1995, only a limited number of prospective studies investigating the relation between physical activity and health outcomes have had adequate samples of non-Hispanic white men or women and one or more other race/ethnicities, which would allow a direct comparison of benefits. In the observational cohort studies with all-cause mortality or cause-specific chronic disease morbidity and mortality as the outcome and with sufficient samples sizes and event rates to have reasonable power to detect meaningful difference between race and ethnic groups, no differences have been reported. In prospective observational studies conducted in countries where the majority of the population is other than non-Hispanic white, the generally favorable relation between higher levels of physical activity and chronic disease events is similar to many of the studies reporting on non-Hispanic white populations. In the few experimental studies where aerobic exercise training was the intervention, no meaningful differences have been reported for changes in cardiorespiratory fitness, body weight, or cardiovascular disease biomarkers when comparing non-Hispanic white and African-American men and women. Thus, based on the currently available scientific evidence, the dose of physical activity that provides various favorable health and fitness outcomes appears to be similar for adults of various races and ethnicities.

Reference List

1. American College of Cardiology, American Heart Association. Methodology manual for ACC/AHA guideline writing committees 2008 [cited 6 A.D. May 23] Available from http://www.americanheart.org/presenter.jhtml?identifier=3039684.

Part F: Scientific Literature Search Methodology

Background

Immediately after HHS Secretary Michael Leavitt announced plans for the development of federal physical activity guidelines on October 27, 2006, the Centers for Disease Control and Prevention (CDC) was assigned to support the Physical Activity Guidelines Advisory Committee's (PAGAC) review of the scientific literature. Working with an advisory committee, staff of the Division of Nutrition, Physical Activity and Obesity (DNPAO) at CDC's National Center for Chronic Disease Prevention and Health Promotion developed a conceptual framework for the literature search. They also established a process to systematically abstract published articles and to make these abstracts readily accessible to PAGAC members and consultants. The product of this effort is called the *Physical Activity Guidelines for Americans* Scientific Database (http://apps.nccd.cdc.gov/PhysicalActivityGuidelines).

Conceptual Framework

The overall conceptual framework for this project is found in Figure F.1. The scientific literature review for *Physical Activity Guidelines for Americans* was initially organized around 8 health outcome domains of interest: Cardiorespiratory Health, Metabolic Health, Mental Health, Musculoskeletal Health, Functional Health, Cancer, All-Cause Mortality, and Adverse Events. Of particular interest was the relevant scientific literature that relates 7 characteristics of physical activity (or exposures) to these health outcomes: intensity, frequency, duration, pattern, type, caloric expenditure, and volume. Also of interest — as related to these physical activity "exposures" — are physiologic states and adaptations to physical activity that may be precursors to the health outcomes listed above.

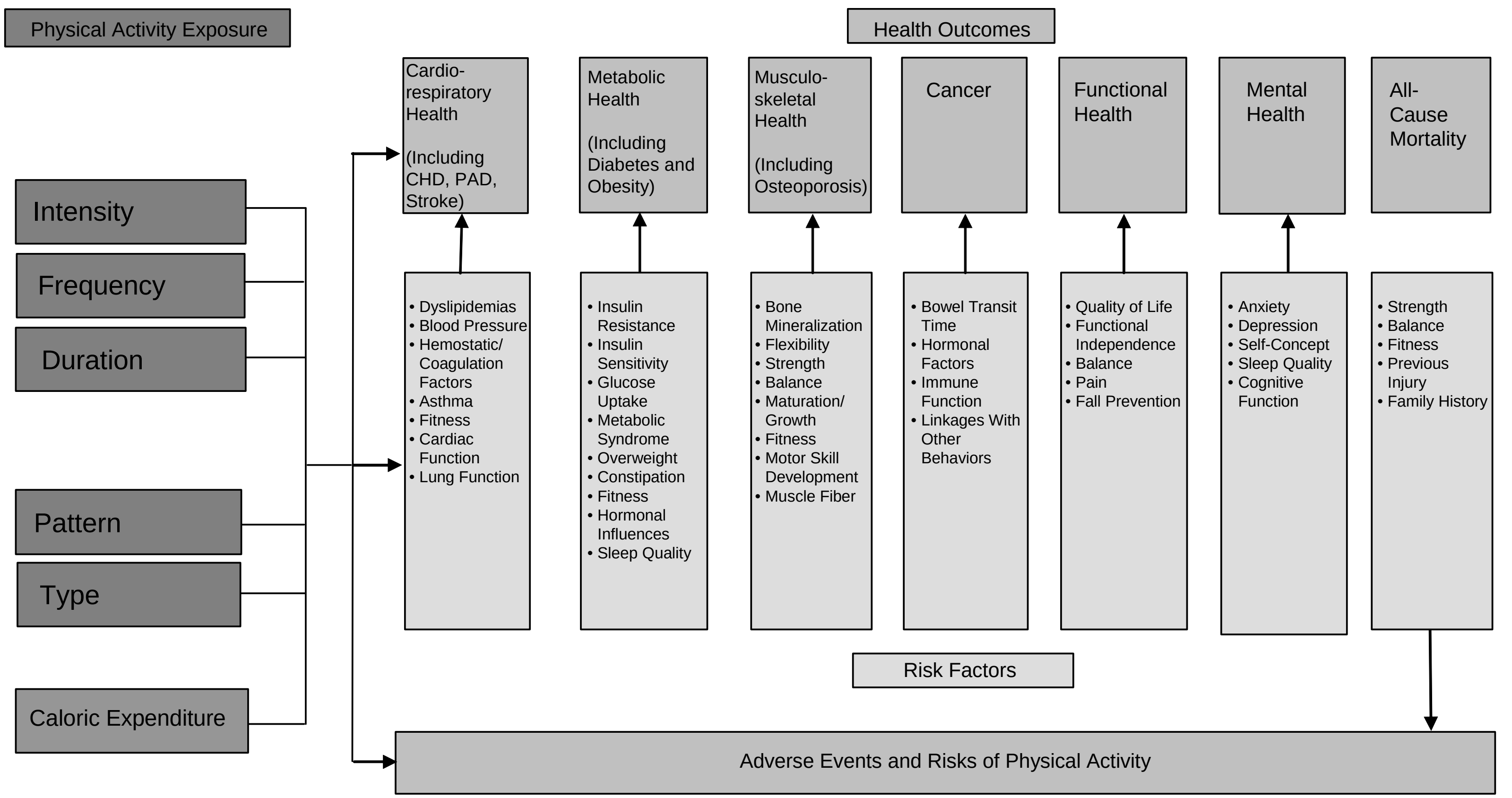
Research Questions

At least 7 key research questions were used to guide the literature review and the deliberations of the PAGAC. For each health outcome of interest:

1. Is there sufficient evidence that physical activity is associated with [Outcome]?

2. Is there sufficient evidence to support differing intensities of physical activity in relation to the association with [Outcome] or precursors?

Figure F.1. *Physical Activity Guidelines for Americans*: Conceptual Framework for Literature Review



All arrows will be examined for heterogeneity across demographic characteristics (e.g., sex, age, race/ethnicity). Evidence will also be examined for select special population groups.

CHD, coronary heart disease; PAD, peripheral arterial disease

3. Is there sufficient evidence that the accumulation of multiple short periods of physical activity is associated with [Outcome] or precursors?

4. Is there sufficient evidence of increased risk with physical activity associated with [Outcome]?

5. Is there sufficient evidence that supports a pattern of weekly regularity (days per week) of physical activity and association with [Outcome] or precursors?

6. Is there sufficient evidence that different modes (types) of physical activity are (differentially and similarly) associated with [Outcome]?

7. Is there sufficient evidence that a physical activity exposure other than 30 minutes per day on most, preferably all, days each week is associated with [Outcome]?

Operational Plan

Following from the conceptual framework, 3 CDC teams were formed to conduct the literature reviews around 3 key life stages: youth (aged 5 to 19 years), adults (aged 19 to 64 years), and older adults (aged 65 years and older). All aspects of the literature review (i.e., search strategy development and execution, review and triage of papers, cataloguing, retrieving, coding, data entry, quality control, and payment of coders) were managed by the teams. Two scientists (one senior, one junior) were appointed as co-leads for each life-stage team, and coders were assigned to the teams based on the review workload (e.g., more studies were available for adults than for youth). In addition, a separate team was formed to develop and implement quality control procedures.

Phase 1 of the literature review process (October 2006 through June 2007) was carried out by conducting systematic searches of the scientific literature on physical activity and the health outcomes described above. During this phase, the teams held weekly meetings to discuss issues that members were encountering and to devise solutions to move the project forward. Issues included literature search terms, inclusion/exclusion criteria for the literature search, study quality assessment, abstraction form and quality control, database/systems issues, abstraction progress, qualifications required of the coders, certification process and selection of coders, training sessions/agenda for abstractors, certificates developed and sent to certified abstractors, retraining issues, termination of abstractors due to production or quality control problems, development of an operations manual, preparation for the PAGAC meetings and materials, health outcome tables, timelines, team reviews, database revisions, subcommittee reviews/updates, and payment of the coders and scientific advisors.

Phase 2 of the literature review process (July 2007 through March 2008) began after the first PAGAC meeting June 28-29, 2007, and was guided by the needs of the PAGAC. During this phase, team members updated the Phase 1 literature review through June 2007 and worked with PAGAC members to obtain scientific papers that were not abstracted during

Phase 1. This process is described in Appendix F.1. (Appendix F.1 can be accessed at http://www.health.gov/paguidelines/report/.

Literature Review

Working from the literature review conceptual framework, the CDC teams performed a standardized review of the scientific literature to provide evidence for the deliberations of the PAGAC.

Searching the MEDLINE Database

The first step of the review process was to gather studies for possible inclusion in the database, using defined search strategies (Appendix F.2, which can be accessed at http://www.health.gov/paguidelines/report/). Search terms were selected for physical activity and for each identified health outcome: cardiovascular and respiratory health, metabolic health, musculoskeletal health, cancer, functional health, mental health, all-cause mortality, and injuries/adverse events.

Using the Ovid interface, the CDC teams searched the National Library of Medicine's (NLM) MEDLINE Database using only Medical Subject Headings (MeSH) major descriptors for the physical activity term set. They used a combination of MeSH descriptors and text word synonyms to search for the health outcome terms set. A listing of all MeSH headings used in the search strategies is included in Appendix F.2.

Three searches were run, and a combination of MeSH headings and text word synonyms were used to limit retrieval to 3 age groups: youth, adults, and older adults. To capture any articles not indexed by age, a fourth search was run, excluding all previous age group retrieval. A fifth search was run, combining all age groups to capture items indexed to multiple age groups. The search strategies for the 5 groups are included in Appendix F.2.

Each search was further limited by restricting retrieval to English language and to articles published after 1994 that dealt with human subjects and contained abstracts. Finally, the searches excluded 3 publication types — comments, editorials, and reviews. Search results were stored in Word files and imported into Reference Manager Database files.

Selecting the Articles

The CDC teams developed specific inclusion and exclusion criteria to determine whether studies would be eligible for abstraction. They also developed an inclusion/exclusion coding system that allowed them to classify references efficiently and accurately for the abstraction process. This process was divided into 2 phases: Certain studies of physical activity and a diagnosable health outcome were abstracted during Phase 1; other studies of physical activity and risk factors for the health outcomes were held for possible abstraction at a later date (Phase 2), if requested by the PAGAC.

Inclusion and Exclusion Criteria

Articles were considered for inclusion in the review if they met certain criteria. Similarly, articles with certain criteria were excluded from the review. Appendix F.3 provides a detailed explanation of the inclusion and exclusion criteria developed for this review. (Appendix F3 can be accessed at http://www.health.gov/paguidelines/report/.)

Abstracting the Articles

For each scientific article, abstractors recorded the following information: Overall study design; sample and participant characteristics; intervention design and duration (if an intervention study); physical activity exposure(s), including the dose of physical activity provided to participants or in which they participated; follow-up time period; health outcome(s); and the most advanced study results. For example, if a study presented an analysis adjusted for age and presented the same analysis adjusted for age and body mass index (BMI), the abstractor was instructed to record the age- and BMI-adjusted results.

Abstractors were hired, trained, and certified to perform all abstracting duties, and strict quality control procedures were used throughout the abstraction project. The quality control team checked and corrected 12.5% of abstracted papers. Abstractors were put on probationary status if they did not meet quality control standards. Cursory checks of abstractions were conducted, and subsequent corrections were made by all members of the Physical Activity Guidelines team at CDC.

A Web-based data entry system was developed to manage all abstracted studies for this project. This system was modeled after a similar system that CDC has used to abstract studies for the *Guide to Community Preventive Services*, which provides systematic reviews of community-based interventions. The physical activity Web-based data entry system includes summary tables of the scientific articles abstracted as part of the literature review for the *Physical Activity Guidelines for Americans.* The summary tables can be accessed at http://apps.nccd.cdc.gov/PhysicalActivityGuidelines.

Part G. Section 1: All-Cause Mortality

Introduction

This chapter examines the relation between physical activity and all-cause mortality. Two leading causes of mortality, both in the United States as well as globally, are cardiovascular disease and cancer, with both diseases estimated to be responsible for 43% of all deaths globally (1). From a biological perspective, the evidence is strongly persuasive that physical activity reduces the occurrence of these leading causes of death (discussed in the individual chapters on these diseases); thus, it is also biologically plausible for physical activity to postpone the occurrence of all-cause mortality. (Because we all die eventually, when the phrase "lower risk of all-cause mortality" is used in this chapter, it refers to lower risk during the period of follow-up in a study; i.e., postponed mortality.)

Review of the Science

Overview of Questions Addressed

This chapter addresses 5 specific questions:

1. Is there an association between physical activity and all-cause mortality? If so, what is the magnitude of this association?

2. What is the minimum amount of physical activity associated with significantly lower risk of all-cause mortality?

3. Is there a dose-response relation between physical activity and all-cause mortality?

4. What is the shape of the dose-response relation between physical activity and all-cause mortality?

5. Is the relation between physical activity and all-cause mortality independent of adiposity?

Data Sources and Process Used to Answer Questions

To provide evidence-based answers to the above questions, the All-cause Mortality subcommittee obtained data from a search of the *Physical Activity Guidelines for Americans* Scientific Database (see ***Part F: Scientific Literature Search Methodology***, for a full description of the database). The Database contains studies published in 1995 and later. The selection criteria were broad and included searching for studies of all age groups, all study designs, and all physical activity types that had the outcome of all-cause mortality. This retrieved 83 publications, of which 7 were excluded for the following reasons: 3 studies of exercise-related mortality were covered in another chapter; 2 studies of survival among cancer patients were covered in another chapter; 1 study provided essentially duplicate results on physical activity and all-cause mortality as another; and 1 study did not provide results on the specific association of physical activity with all-cause mortality. An additional 3 studies of cardiovascular or muscular fitness in relation to all-cause mortality were excluded because, although they provided important information, they did not directly inform on the amount of physical activity associated with decreased risk of premature mortality (additional discussion of studies on physical fitness and all-cause mortality is provided later in this chapter). This left 73 studies that provide the evidence based for the conclusions of this chapter. (Table G1.A1, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.)

Question 1: Is There an Association Between Physical Activity and All-Cause Mortality? If So, What Is the Magnitude of This Association?

Conclusions

The data very strongly support an inverse association between physical activity and all-cause mortality. Active individuals — both men and women — have approximately a 30% lower risk of dying during follow-up, compared with inactive individuals. This inverse association has been observed among persons residing in the United States, as well as in other countries, older persons (aged 65 years and older), and persons of different race/ethnic groups. In one study of persons with impaired mobility (unable to walk 2 km and climb 1 flight with no difficulty), physical activity also appeared to be associated with lower all-cause mortality rates.

Rationale

Description of Studies in Evidence Base

Of the 73 studies included in the evidence base (Table G1.A1), 71 were prospective cohort studies, 1 was a retrospective cohort study, and 1 was a case-control study. These studies were conducted in many countries in North America, Europe, the Middle East, Asia, and Australia. Twenty-seven studies, or 37%, were studies in the United States; the remaining 46 (63%) were conducted in other countries. The length of follow-up in the studies ranged from 10 months to 28 years, apart from the one retrospective cohort study of Finnish Olympic athletes, in which follow-up was 71 years (2). Across all studies, the median follow-up was 11.7 years.

Population Subgroups

These studies provide a large database that included 312,554 observations in men and 690,671 observations in women, with a total of 140,114 deaths. Because several studies published updated results in the same subjects, unique observations totaled 254,514 men and 576,574 women, and 113,358 deaths. Although the total number of women is larger than the total number of men, this is skewed by 3 large studies of women (3-5); actually, fewer studies included women (n=51), compared with studies that included men (n=62).

The youngest subjects included were aged 16 years (6), though most studies (44 of 73 studies, or 60%) included middle-aged subjects aged 40 years and older. A reasonable body of evidence was specific to older persons aged 65 years and older, with 15 studies including such subjects. With regard to race/ethnicity, among the US studies, most included only small proportions of persons belonging to race/ethnic minority groups. However, 3 included nationally representative samples of subjects (7-9) and another comprised 48.3% blacks (10). In addition, 2 studies specifically enrolled Hispanic-American (11) and Japanese-American men (12); 5 studies conducted in Asia enrolled Chinese and Japanese subjects (4;13-16).

Most of the studies enrolled ostensibly healthy subjects who were free of cardiovascular disease and cancer. However, several studies did select patient groups, including patients with coronary artery disease (17) or at high risk (9;18), and patients with diabetes. (7;19-22). In one study, subjects with impaired mobility were examined separately (23).

Main Findings

The available data strongly support an inverse relation between physical activity and all-cause mortality rates during follow-up, with 67 of the 73 studies reporting a significant, inverse relation for at least one group of subjects (e.g., men versus women) and/or one domain of activity (e.g., all activity, exercise activity, or commuting activity).

With regard to the strength of association, the median relative risk (RR), comparing most with least active subjects was 0.69 across all studies, indicating a 31% risk reduction with physical activity. This was similar for men (median RR = 0.71) and women (median RR = 0.67), and for studies where both sexes were analyzed together (median RR = 0.68). The magnitude of association in this evidence base, which included studies published in 1995 and later, is similar to that reported in a 2001 review that included studies published before 1995 (24).

An inverse association also existed among persons aged 65 years and older, with a median relative risk of 0.56 when comparing most with least active persons. No significant interaction was observed with race/ethnic groups in a study that included nationally representative subjects (i.e., results did not differ across race/ethnic groups) (7). Inverse associations also were noted among Puerto Rican men (11), Japanese-American men (12), and Chinese and Japanese men and women living in Asia (4;13-16). Additionally, inverse relations between physical activity and all-cause mortality were reported among patients with coronary artery disease (17) or at high risk (9;18), and among patients with diabetes (7;19-22). One study examined subjects with and without impaired mobility separately. Among persons with impaired mobility, mortality rates also appeared lower among active than inactive persons (this was not directly tested for statistical significance) (23).

Validity of Findings

Because all of the studies in the evidence base were observational epidemiologic studies with no randomized controlled trials, the data cannot prove causality of effect. However, the totality of evidence does support a cause-and-effect relation between physical activity and lower all-cause mortality rates for the following reasons. First, as mentioned above, plausible biological mechanisms — demonstrated in randomized clinical trials — exist for physical activity to decrease the occurrence of cardiovascular disease and cancer, the leading causes of mortality worldwide.

Second, bias due to decreased physical activity from ill health (i.e., a spurious inverse relation, with ill health causing decreased physical activity, rather than physical activity causing lower mortality rates) is unlikely. Many of the studies in Table G1.A1 included only ostensibly healthy subjects and excluded persons with cardiovascular disease and cancer. Studies that did include subjects with chronic diseases typically adjusted for the presence of these conditions, and continued to observe inverse associations between physical activity and all-cause mortality rates. Several studies also allowed for a lag period (i.e., excluding initial years of follow-up) in analyses to minimize the potential bias from ill health leading to decreased physical activity (as ill persons are likely to die early in follow-up); physical activity was significantly related to lower all-cause mortality rates in these analyses. Finally, if the follow-up period is long (which was typically the case, with the median follow-up being 11.7 years), the impact of this bias will be diluted, with ill persons dying early in follow-up.

Third, bias due to systematic misclassification of physical activity is unlikely. It is true that almost all of the studies collected physical activity information using self-reports by subjects, and this is likely to be imprecise. However, because physical activity was assessed prospectively in almost all the studies, any misclassification is likely to be random (leading to dilution of results, rather than a systematic bias). Additionally, one study assessed physical activity using doubly-labeled water, considered a gold standard for measuring energy expenditure. This study did report an inverse relation between physical activity and all-cause mortality rates (10).

Fourth, bias resulting from large losses to follow-up is unlikely. Although many studies did not report follow-up rates, many of these studies used national systems to ascertain deaths (e.g., National Death Index in the United States), which tend to be complete. Of the studies that did report follow-up rates, these tended to be very high.

Finally, physically active persons tend to have other healthy habits as well, which may confound the association of physical activity with all-cause mortality rates. This is unlikely to have explained the inverse relation observed because the association persisted after controlling for several potential confounders (including age, sex, race, education, smoking, body mass index [BMI], alcohol, diet, personal and family medical history, and reproductive variables in women) listed in Table G1.A1.

Physical Fitness and All-Cause Mortality

Studies of physical fitness and all-cause mortality were not reviewed in the same detail as studies of physical activity because the former studies do not provide direct information that can be translated to public health recommendations for physical activity (e.g., How much? What intensity? What duration? What frequency?). However, physical fitness, which includes cardiorespiratory fitness, is closely related to physical activity. In particular, among most individuals and particularly in those who are sedentary, increases in physical activity result in increases in cardiorespiratory fitness. Thus, cardiorespiratory fitness is an objective and reproducible marker of recent physical activity patterns. The findings from studies of cardiorespiratory fitness mirror those from studies of physical activity in showing inverse associations with all-cause mortality (see ***Part G. Section 2: Cardiorespiratory Health*** for a detailed discussion of this issue). In fact, the magnitude of association is stronger for studies of cardiorespiratory fitness, which may be due in part to the higher precision of measurement, as, most of these studies use objective measurements of fitness (instead of, typically, self-reported physical activity). For example, in the Aerobics Center Longitudinal Study, the relative risks for mortality among the most fit men and women were 0.49 and 0.37, respectively, while the associations for physical activity were much weaker (25). In a recent review (26), the median relative risk for all-cause mortality, comparing most fit with least fit men in 10 studies was 0.55; for women in 6 studies, this also was 0.55. Thus, the findings from studies of physical fitness support those from studies of physical activity, with regard to an inverse relation with all-cause mortality.

Question 2: What Is the Minimum Amount of Physical Activity Associated With Significantly Lower Risk of All-Cause Mortality?

Conclusions

The studies in the evidence base have assessed different domains of physical activity (including one of more of the following: leisure-time activity, occupational activity, household activity, and commuting activity), with most assessing primarily leisure-time physical activity (LTPA), including walking. Some evidence indicates that it may be the overall **volume** of energy expended — regardless of which activities produce this energy expenditure — that is important to lower the risk of mortality. The studies also have used different measures or units, such as kilocalories per week, metabolic equivalent (MET)-hours per week, or hours per week to categorize physical activity levels in analyses. Thus, combining the findings across studies posed a challenge.

In synthesizing the data across studies and expressing their findings in a fashion that can be readily translated for public health purposes, the evidence base is clear in showing that the equivalent of at least 2 to 2.5 hours per week of moderate-intensity physical activity is sufficient to significantly decrease all-cause mortality rates (see Table G1.1, below). Several studies investigated walking specifically, and it is reasonably clear that walking 2 or more hours per week is associated with a significantly lower risk of all-cause mortality (see Table G1.2, below). Additionally, faster pace of walking, compared with slower pace, is associated with lower risk.

Table G1.1. Minimum Amounts of Physical Activity Associated With Significantly Lower Risks of All-Cause Mortality

The data are presented according to different classifications of physical activity in the studies reviewed. Within each classification scheme, studies are ordered according to their findings regarding the minimum amount of activity observed to be associated with significantly lower risk of all-cause mortality (lowest to highest).

Studies with subjects classified by **energy expended** in physical activity:

Reference	Men	Women	Both Sexes Analyzed Together
Yu et al., 2003 (27)	23.9-2142.9 kcal/day vigorous LTPA (vs. 0-0.6 kcal/day)	–	–
Lee et al., 1995 (28)	750-1499 kcal/wk vigorous LTPA (vs. <150 kcal/wk)	–	–
Tanasescu et al., 2003 (22)	12.1-21.7 MET-hr/wk LTPA (vs. 0-5.1 MET-hr/wk); ≥16.1 MET-hr/wk walking (vs. 0-1.4)	–	–
Bucksch 2005 (29)	–	14-<33.5 kcal/kg/wk LTPA; i.e., ~910-2200 kcal/wk (65 kg woman) (vs. 0 kcal/kg/wk)	–
Fried et al., 1998 (30)	–	–	980-1890 kcal/wk LTPA (vs. ≤67.5 kcal/wk)
Lee & Paffenbarger 2000 (31)	1000-1999 kcal/wk LTPA (vs. < 1000 kcal/wk)	–	–
Janssen & Jolliffe 2006 (17)	–	–	1000-1999 kcal/wk LTPA (vs. < 500 kcal/wk)

Table G1.1. Minimum Amounts of Physical Activity Associated With Significantly Lower Risks of All-Cause Mortality (continued)

Studies with subjects classified by **energy expended** in physical activity (continued):

Reference	Men	Women	Both Sexes Analyzed Together
Lan et al., 2006 (15)	–	–	1000-1999 kcal/wk LTPA (vs. < sedentary)
Haapanen et al., 1996 (32)	>2100 kcal/wk LTPA, household activities, commuting (vs. <800 kcal/wk)	–	–
Matthews et al., 2007 (4)	–	10.0-13.6 MET-hr/day LTPA, work, household, walking/ cycling commute (vs. ≤9.9 MET-hr/day)	–
Manini et al., 2006 (10)	–	–	>770 kcal/day all activities (doubly-labeled water) (vs. <521 kcal/day)
Carlsson et al., 2006 (33)	–	>50 MET-hr/day LTPA, work, household, walking/cycling (vs. <35 MET-hr/day)	–

Studies with subjects classified by **duration** of physical activity:

Reference	Men	Women	Both Sexes Analyzed Together
Bijnen et al.,1999 (34)	At least 20 min/day, 3 day/wk walking and cycling (vs. lesser amount)	–	–
Rockhill et al., 2001 (35)	–	1-1.9 hr/wk moderate- to vigorous LTPA (vs. <1 hr/wk)	–
Gregg et al., 2003 (7)	–	–	≥2 hr/wk walking (vs. none) ≥2 hr/wk LTPA (vs. none)
Landi et al., 2004 (36)	–	–	≥2 hr/wk LTPA and chores (vs. <2 hr/wk)

Table G1.1. Minimum amounts of physical activity associated with significantly lower risks of all-cause mortality (continued)

Studies with subjects classified by **duration** of physical activity (continued):

Reference	Men	Women	Both Sexes Analyzed Together
Mensink et al., 1996 (37)	>2 hr/wk sports (vs. none)	–	–
Leon et al., 1997 (18)	140 min/day LTPA (vs. 4.9 min/day)	–	–
Schooling et al., 2006 (16)	–	–	≤30 min/day LTPA (vs. none)
Hu et al., 2004a (3)	–	≥3.5 hr/wk moderate-to vigorous LTPA (vs. ≤0.5 hr/wk)	–
Fujita et al., 2004 (13)	–	≥1 hr/day walking (vs. ≤0.5 hr/day)	–

Studies with subjects classified by **frequency** of physical activity:

Reference	Men	Women	Both Sexes Analyzed Together
Sundquist et al., 2004 (38)	–	–	Occasional LPTA (vs. none)
Lam et al., 2004 (14)	1/mo to 1-3/wk LTPA of ≥30 min (vs. <1/mo)	1/mo to 1-3/wk LTPA of ≥30 min (vs. <1/mo)	–
Kushi et al., 1997 (39)	–	Few/mo to 1/wk to moderate LPTA (vs. never/rarely)	–
Hillsdon et al., 2004 (40)	–	–	1/wk vigorous sports/recreation (vs. <1/mo)

LTPA, leisure-time physical activity

Table G1.2. Walking and All-Cause Mortality

For each study, the data* presented are for the lowest walking level significantly associated with decreased relative risk of all-cause mortality. For studies without significant results, the non-significant relative risk (shown in ***bold italics***) associated with the highest walking level is given.

Further, the studies are grouped according to different classifications of walking in the studies reviewed. Within each classification scheme for walking, studies are ordered from lowest to highest walking level.

Table G1.2. Walking and All-Cause Mortality (continued)

Studies with subjects classified by **energy expended** on walking:

Reference	Men	Women	Both Sexes Analyzed Together
Tanasescu et al., 2003 (22)	≥16.1 MET-hr/wk (vs. 0-1.4): RR = 0.60 (0.41-0.88)	–	–
Matthews et al., 2007 (4)	–	≥7.1 MET-hr/day (vs. 0.3.4): RR = 0.86 (0.75-1.05)	–

Studies with subjects classified by **time** spent walking:

Reference	Men	Women	Both Sexes Analyzed Together
Gregg et al., 2003 (7)	≥2 hr/wk (vs. 0): RR = 0.61 (0.48-0.78)	≥2 hr/wk (vs. 0): RR = 0.71 (0.59-0.87)	–
Stessman et al., 2000 (41)	–	–	~4 hr/wk (vs. <4 hr/wk): RR = 0.41 (0.19-0.91)
LaCroix et al., 1996 (42)	–	–	>4 hr/wk: ***RR = 0.91 (0.58-1.42)***
Fujita et al., 2004 (13)	≥1 hr/day (vs. ≤0.5): ***RR = 0.91 (0.80-1.04)***	≥1 hr/day (vs. ≤0.5): RR = 0.75 (0.62-0.90)	–
Wannamethee et al., 1998 (43)	>60 min/day (vs. 0): ***RR = 0.62 (0.37-1.05)***	–	–
Schnohr et al., 2007 (44)	>2 hr/day (vs. <0.5): ***RR = 0.80 (0.59-1.10)***	>2 hr/day (vs. <0.5): ***RR = 0.89 (0.69-1.14)***	–

Studies with subjects classified by **distance** walked:

Reference	Men	Women	Both Sexes Analyzed Together
Smith et al., 2007 (21)	–	–	≥1 mile/day (vs. 0): ***RR = 0.89 (0.67-1.18), normoglycemics*** RR = 0.54 (0.33-0.88), diabetics
Hakim et al., 1998 (12)	1.0-2.0 miles/day (vs. <1) RR = 0.68 (no CI provided)	–	–

Table G1.2. Walking and All-Cause Mortality (continued)

Studies with subjects classified by **distance** walked (continued):

Reference	Men	Women	Both Sexes Analyzed Together
Lee & Paffenbarger 2000 (31)	≥12.5 miles/wk (vs. <3.1): RR = 0.84 (0.75-0.94)	–	–

Studies with subjects classified by **pace** of walking:

Reference	Men	Women	Both Sexes Analyzed Together
Davey Smith et al., 2000; (45) Batty et al., 2002; (19) Batty et al., 2003 (46)	P, trend across slower, the same, faster pace (compared to others) all < 0.01	–	–
Schnohr et al., 2007 (44)	Average walking pace (vs. slow): RR = 0.75 (0.61-0.92)	Average walking pace (vs. slow): RR = 0.54 (0.45-0.67)	–

Studies with subjects classified by **walking/cycling** combined:

Reference	Men	Women	Both Sexes Analyzed Together
Bijnen et al., 1998 (47)	≥20 min, 3 days/wk: RR = 0.71 (0.58-0.88)	–	–
Barengo et al., 2004 (48)	≥30 min/day commute (vs. <15): ***RR = 1.07 (0.98-1.17)***	≥30 min/day commute (vs. <15): ***RR = 0.98 (0.88-1.09)***	–
Hu et al., 2004b (20)	–	–	≥30 min/day commute (vs. 0): ***RR = 0.88 (0.75-1.04)***
Carlsson et al., 2006 (33)	–	>1.5 hr/day (vs. almost never): RR = 0.58 (0.45-0.75)	–

*Data shown are relative risk, RR (95% CI).

It is important to note that this amount — 2 to 2.5 hours per week of moderate-intensity physical activity — does not represent a threshold level for risk reduction. Rather, the data consistently support an inverse dose-response relation for the total volume of energy expended, supporting a "some is good; more is better" message (see discussion under Question 3 below).

Rationale

Assessment of Physical Activity

The different studies reviewed in this chapter primarily have used questionnaires to assess physical activity. These questionnaires were different across the various studies and assessed one or more domains of physical activity — leisure-time, household, occupation, and commuting activity — with most assessing primarily leisure-time physical activity. In analyses, the studies classified subjects using different classification schemes, such as by energy expended, duration of activity, and frequency of activity. Several studies classified subjects by ordinal groupings of physical activity (e.g., groups denoted as "sedentary," "light," "moderate," and "heavy"), but the amount of activity attributable to each category was unclear. Thus, combining the data across studies and translating the findings into a fashion that could be readily translated for public health purposes was challenging. Future studies should attempt to collect detailed information on physical activity, as well as categorize this in ways that make comparison across studies feasible. One helpful strategy may be to use standardized units, such as energy expenditure (e.g., MET-hours per week) of duration in activities of specified intensity (e.g., hours per week of moderate-intensity physical activity).

Minimum Amount of Physical Activity Needed

Table G1.1 lists the studies with quantifiable amounts of physical activity, and shows that most of the physical activity assessments were derived from leisure-time activities. For studies classifying subjects by energy expended, it appears that some 1,000 kilocalories per week or 10 to 12 MET-hours per week (approximately equivalent to 2.5 hours per week of moderate-intensity activity) or more is needed to significantly lower the risk of all-cause mortality. For studies classifying subjects by the duration of their physical activity, it appears that some 2 hours per week or more is needed for significantly lower risks. A few studies classified subjects by the frequency of physical activity (with or without duration built in). These sparse data show that even 1 per month to 1 to 3 times per week of physical activity, lasting at least 30 minutes in duration, is significantly associated with lower risk. Across all studies, the minimum amount of activity did not appear to differ for men and women.

Walking

Many studies have included walking in their assessment of physical activity, although several combined this activity into an overall estimate of physical activity (e.g., as kilocalorie energy expenditure). In recent years, however, investigators have been interested in walking as an activity to be promoted for public health, and several studies have presented data specifically on walking in relation to all-cause mortality rates.

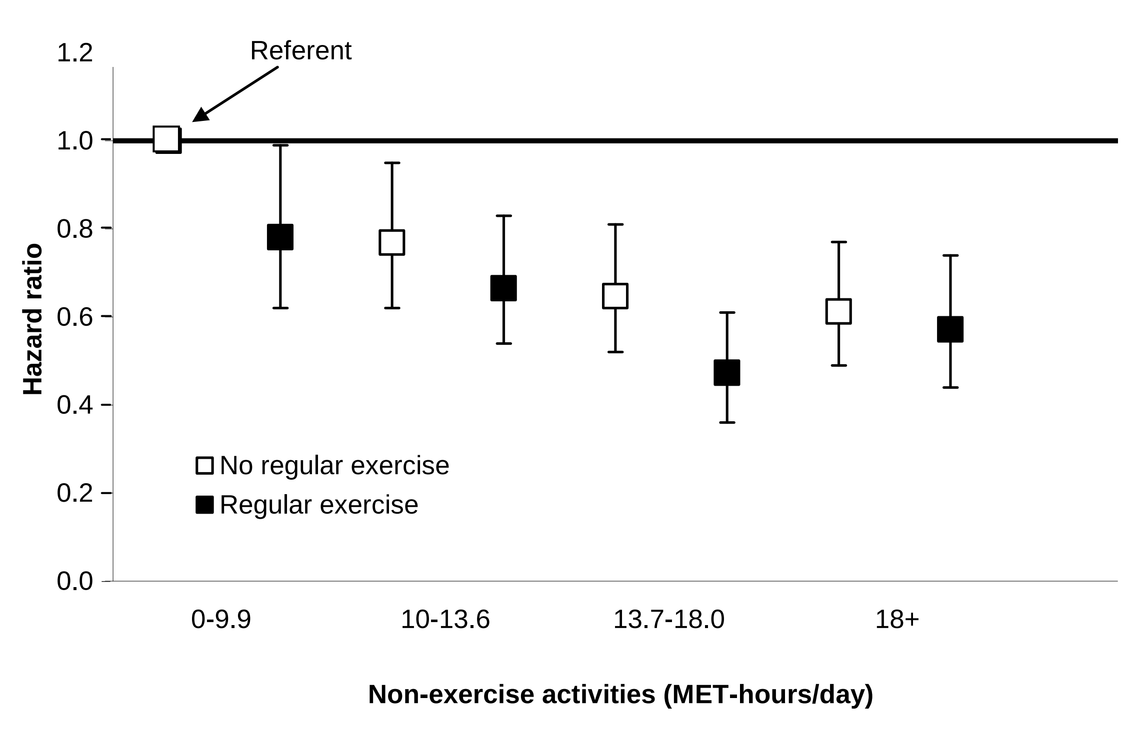
Table G1.2 summarizes the findings from studies that have specifically investigated walking. In these studies, investigators classified walking according to the energy expended on walking, the time spent walking, the distance walked, the pace of walking, and walking combined with bicycling, primarily for the purpose of commuting. Only 2 studies examined the energy expended on walking and all-cause mortality rates; the data are inconsistent. With regard to the time spent walking, for which most data are available, the findings are reasonably consistent in showing that walking some 2 or more hours per week is associated with a significantly lower risk. A small body of data suggests that walking 1 to 2 miles per day is associated with lower risk. Additionally, faster pace of walking, compared with slower pace, is consistently associated with lower risk. Few data are available on walking or cycling as part of active commuting in relation to all-cause mortality, with investigators typically examining 30 minutes or more per day of active commuting versus lesser levels. These data are inconsistent and do not indicate that 30 minutes or more per day of active commuting is associated with lower risk.

What Activities "Count"?

As mentioned previously, the studies reviewed in this chapter that have shown an inverse relation between physical activity and all-cause mortality primarily have assessed leisure-time physical activity, including walking. However, some evidence indicates that it may be the overall **volume** of energy expended — regardless of where this energy is derived —that is important to lower the risk of mortality. Studies that have attempted to assess the total amount of energy expended in leisure-time, occupational, household activity, and commuting activity have reported significant inverse associations with the overall volume of physical activity, as well with most of the individual domains analyzed separately (except for commuting activity). These studies have included the Swedish Mammography Cohort Study (33) and the Shanghai Women's Health Study (4). In the Shanghai Women's Health Study (Figure G1.1), as amounts of energy expended on what investigators termed "nonexercise activities" (i.e., activities other than leisure-time activity, including household chores, walking and cycling as part of commuting, and climbing stairs) increased, rates of all-cause mortality declined steadily.

Within each category of "nonexercise activities," the addition of "regular exercise" (i.e., regular leisure-time physical activity) further reduced risk, except at the highest level of nonexercise energy expenditure. This observation is compatible with the postulated dose-response relation between physical activity and all-cause mortality, described in detail under Questions 3 and 4 below. That is, the dose-response is likely curvilinear such that at higher levels of energy expended, the curve flattens out. So in the Shanghai Women's Health Study, women at the highest level of nonexercise activities may have been at the upper end of the dose-response curve, and the addition of further amounts of energy expended on exercise activities did not appreciably reduce all-cause mortality rates further.

Figure G1.1. Relative risks of all-cause mortality according to exercise and nonexercise activities, Shanghai Women's Health Study



Source: Matthews et al., 2007 (4), with permission

Values are hazard ratios and 95% confidence intervals.

Adjusted for age (years), marital status (yes, no), education (elementary school or less, junior high school, high school, college/post-high school), household income (low, middle, high), smoking (ever, never), alcohol drinking (ever, never), number of pregnancies, oral contraceptive use (ever, never), menopausal status (yes, no), and several chronic medical conditions, such as diabetes (yes, no), hypertension (yes, no), respiratory disease (yes, no; asthma, chronic bronchitis, or tuberculosis), and chronic hepatitis (yes, no).

Figure G1.1. Data Points

Non-exercise activities (MET-hrs/d)	No regular exercise Hazard Ratio	No regular exercise (95% CI)	Regular exercise Hazard Ratio	Regular exercise (95% CI)
0–9.9	1.00	–	0.78	(0.62–0.99)
10–13.6	0.77	(0.62–0.95)	0.67	(0.54–0.83)
13.7–18.0	0.65	(0.52–0.81)	0.47	(0.36–0.61)
18.1+	0.61	(0.49–0.77)	0.57	(0.44–0.74)

Further support for the premise that all activities "count," and that it is the total amount of energy expended that is relevant for all-cause mortality, comes from the Health ABC study (10). In this study, which objectively measured total energy expenditure using doubly-labeled water, the relative risk for all-cause mortality was significantly lower (0.65) among men and women who expended more than 770 kilocalories per day in physical activity, compared with less than 521 kilocalories per day. (The energy expended in physical activity was estimated as: [total energy expenditure*0.90] — resting metabolic rate; i.e., assuming the thermic effect of food to be 10%.) Among those expending 521 to 770 kilocalories per day, the relative risk was 0.64, well below 1.0 but not statistically significant, which is a likely consequence of reduced power due to the small number of deaths (n=55) in this study.

Findings from Studies of Physical Fitness That Can Inform on the Minimum Amount of Physical Activity Needed

As stated previously, studies of cardiorespiratory fitness and all-cause mortality do not provide direct information on the minimum amount of physical activity needed. However, these studies can provide indirect information, in that the physical activity levels of groups of fit subjects, who have lower mortality rates compared with unfit subjects, can be ascertained. In a large prospective cohort study where moderate and high levels of cardiorespiratory fitness were associated with lower rates of all-cause mortality, compared with low levels of fitness in both men and women, the physical activity levels of subjects were obtained by questionnaire (49). Men in the moderate and high cardiorespiratory fitness groups reported an average of 130 and 138 minutes per week of walking, respectively. Among women, the corresponding amounts were 148 and 167 minutes per week, respectively. Thus, these data are compatible with data from the overall body of literature on physical activity and all-cause mortality, which suggest that walking at least 2 hours per week is needed to significantly lower mortality rates.

Question 3: Is There a Dose-Response Relation Between Physical Activity and All-Cause Mortality?

Conclusions

The dose-response relation can be assessed with respect to specific dimensions of physical activity, such as the total volume of energy expended, the intensity of the physical activity carried out, the duration of physical activity, or the frequency of physical activity. The largest amount of data, as well as the clearest, pertains to the total volume of energy expended. These data consistently show an inverse dose-response relation between volume of energy expended and all-cause mortality. Thus, while the answer to Question 2 above indicates that at least 2 to 2.5 hours per week of moderate-intensity physical activity is needed to significantly decrease all-cause mortality rates, this amount does not represent a minimum threshold level for risk reduction. Rather, the dose-response relation for the total volume of energy expended supports a "some is good; more is better" message. Some data indicate that among populations where physical activity levels are likely to be low (e.g., middle-aged and older women, older men), significantly lower mortality rates are observed at levels below 2 to 2.5 hours per week of moderate-intensity physical activity. Taken as a whole, the data support a target of 2 to 2.5 hours per week of moderate-intensity physical activity for lowering all-cause mortality rates, yet also encourage any level of activity below the target for inactive groups of individuals.

Limited data suggest that vigorous-intensity physical activity is associated with additional risk reduction compared with lower-intensity activities, beyond its contribution to the total energy expended. There are no data to clarify dose-response relations for duration and frequency of physical activity that are independent of their contributions to the total volume of energy expended. In other words, it is unknown whether multiple, short bouts of physical activity versus a single, long bout that expends the same energy are differentially associated with all-cause mortality rates.

Rationale

The concept of “physical activity” is complex, in that it includes many different aspects, such as the kinds of activities carried out, the intensity with which they are conducted, and their duration and frequency. In examining the dose-response relation between physical activity and all-cause mortality, we can investigate the association with regard to several specific dimensions of physical activity: the total volume of energy expended, the intensity, the duration, or the frequency. The dose-response relation for each of these dimensions is discussed separately below.

Dose-Response Relation for Total Volume of Physical Activity

As Table G1.A1 indicates, the studies reviewed have used different methods (primarily questionnaires, which differed across studies) to assess physical activity. However, all of them possessed a measure that reflected the total volume of energy expended. This is because any assessment of physical activity, no matter how simple, provides some indication of the total volume of energy expended. For example, in the NHANES I Epidemiologic Follow-up Study (50), physical activity during recreation was assessed by asking, “Do you get much exercise in things you do for recreation, or hardly any exercise, or in between?” Response options were: much exercise, moderate exercise, and little or no exercise. Although it is impossible to equate the different activity categories to actual kilocalories or MET-hours of energy expended, it is clear that the categories represent ordered levels representing the total volume of physical activity.

Of the studies reviewed, 59 of the 73 studies classified subjects according to at least 3 levels of physical activity, allowing for assessment of dose-response related to the total volume of energy expended. Among these 59 studies, 33 reported significant, inverse trends between physical activity and all-cause mortality rates. Another 21 studies showed apparent inverse trends that were not formally tested for statistical significance. The remaining 5 studies showed a non-significant trend (n=1) or apparent lack of trends that were not formally tested for significance (n=4).

As discussed above under Question 2, at least 2 to 2.5 hours per week of moderate-intensity physical activity is needed to significantly decrease all-cause mortality rates. However, rather than representing a minimum threshold level for risk reduction, the dose-response relation for the total volume of energy expended indicates that though this is a desired minimum level of physical activity, risk reductions already begin to occur below this level, supporting a message of “some is good; more is better.” Additionally, some data indicate that among populations where physical activity levels are likely to be low (e.g., middle-aged and older women, older men) significantly lower mortality rates are observed at levels below 2 to 2.5 hours per week of moderate-intensity physical activity. In a study of middle-aged and older women, significantly lower rates of mortality were observed among women engaging in 1 to 1.9 hours per week of moderate-to-vigorous intensity leisure-time physical activity (35). In another study of older men and women aged 65 years and older, “occasional” leisure-time physical activity also was associated with significantly lower mortality rates (38). This association also held true for walking or cycling for at least 20 minutes, 3 days a week, among men aged 64 to 84 years (47).

Further support for the “some is good; more is better” message comes from a recent randomized clinical trial of physical activity to increase cardiorespiratory fitness levels — higher levels of which are associated with lower all-cause mortality rates — among sedentary, postmenopausal women (51). In this trial, a dose-response relation was observed such that graded increased in fitness were observed for 3 groups exercising at 50%, 100%, and 150% of the Surgeon-General’s recommendation (with 100% being equivalent to 150 minutes per week of moderate-intensity physical activity). Thus, these data support a target of 2 to 2.5 hours per week of moderate-intensity physical activity for lowering all-cause mortality rates, yet also encouraging any level of activity below the target for inactive groups of individuals.

Dose-Response Relation for Intensity of Physical Activity

In 11 studies, investigators examined the dose-response relation for intensity of physical activity. All but one reported significantly reduced risks for vigorous-intensity activity compared with lesser-intensity physical activity. However, the interpretation of these findings is not straightforward because the intensity of physical activity is related to the total volume of energy expended. That is, when carried out for the same total duration, higher-intensity physical activities expend more total energy than do lower-intensity physical activities. Thus, if studies do not account for this correlation, it is unclear whether the significantly reduced risk associated with vigorous-intensity physical activity can be attributed to the **intensity** of the activity, or whether it is merely due to the increase in the total **volume** of energy expended (i.e., confounding of intensity by volume of energy expended). In other words, for the same volume of energy expended, does vigorous intensity activity confer additional benefits compared to moderate- or light-intensity activity?

Of the 11 studies, 4 did attempt to account for confounding by the volume of energy expended. All 4 reported significant, inverse dose-response relations with intensity of physical activity. Thus, these limited data suggest that higher intensities of physical activity are associated with additional risk reductions for all-cause mortality, beyond their contribution to greater total volume of energy expended.

Dose-Response Relation for Duration and Frequency of Physical Activity

Longer duration of physical activity, as well as greater frequency of physical activity, results in greater total volume of energy expended, compared with shorter durations or lower frequencies of activity. However, just as with the dose-response relation to the intensity of physical activity, the relation between dose and duration or frequency has the potential to be confounded by the total volume of energy expended. Therefore, the total volume must be taken into account in order to make conclusions regarding duration and frequency that are independent of the total volume of energy expended.

Ten studies examined the dose-response relation between duration of physical activity and all-cause mortality. These studies indicated that longer durations of activity were associated with lower mortality rates. However, these studies did not adjust for confounding by volume of physical activity and so the data on duration may be reflecting the dose-response relation between the total volume of energy expended and risk of all-cause mortality. These data cannot provide any conclusion regarding whether multiple, short bouts of physical activity versus a single, long bout that expends the same energy are differentially associated with all-cause mortality rates.

Three studies examined the dose-response relation for frequency of physical activity. Again, these studies did not adjust for confounding by volume of physical activity; thus, the data on frequency may be reflecting findings for the dose-response of total volume of energy expended and all-cause mortality rates. These data also cannot clarify the relative benefits of multiple, short bouts of physical activity versus a single, long bout that expends the same energy for all-cause mortality rates.

Finally, 1 study examined the association of all-cause mortality and physical activity carried out 1 to 2 days a week and that generates sufficient energy expenditure to meet current physical activity recommendations (i.e., the so-called “weekend warrior” pattern) (52). Overall, the relative risk for mortality among weekend warriors, compared with sedentary men, was 0.85 (95% confidence interval [CI], 0.65, 1.11). In stratified analysis, however, among men without major cardiovascular risk factors, weekend warriors had a significantly lower risk of dying, compared with sedentary men (RR = 0.41 [0.21, 0.81]). This was not seen among men with at least 1 major risk factor (corresponding RR = 1.02 [0.75, 1.38]).

Question 4: What Is the Shape of the Dose-Response Relation Between Physical Activity and All-Cause Mortality?

Conclusions

The dose-response curve relating different amounts of physical activity to all-cause mortality rates appears curvilinear. On average across studies, compared to less than

0.5 hours per week of moderate-to-vigorous physical activity, engaging in approximately 1.5 hours per week of such activity is associated with about a 20% reduction in risk. Additional amounts of activity are associated with additional risk reductions, but at smaller magnitudes, such that an additional approximately 5.5 hours per week is required to observe a further 20% in risk (i.e., approximately 7.0 hours per week is associated with about a 40% reduction in risk, compared with less than 0.5 hour per week).

Rationale

To describe the dose-response curve in detail, studies in which subjects were classified into at least 5 categories of physical activity were selected. Eleven studies defined 5 levels of physical activity; one defined 6 levels. Figure G1.2 shows the dose-response curve for each of the 12 studies. These categories were defined according to ordinal levels of activity (5;43), the frequency of activity (38), the time per week spent in physical activity (35), or the energy expended on physical activity (either as kilocalories per week, MET-hours per week, or MET-hours per day)(15;17;22;28;30;31;33;53). In a first analysis, we did not attempt to quantify the amount of physical activity, but merely designated these categories as 1 to 6, and plotted the relative risks of all-cause mortality associated with each of these categories. In general, these studies support a curvilinear shape to the dose-response curve.

Next, we attempted to synthesize the results across the different studies to obtain an "average" shape of the dose-response curve. Because the physical activity categories represented different amounts of physical activity, we translated them, where possible, into a common measure of hours per week spent on moderate-to-vigorous physical activity. We excluded from the analysis the one study that had 6 categories of physical activity because it used ordinal groupings that did not allow interpretation of the amount of physical activity. For the remaining studies, we assigned to each of their 5 categories of physical activity the median value of that category, in hours per week of moderate-to-vigorous physical activity. We plotted the median relative risk of all-cause mortality against each of these 5 categories of physical activity.

Figure G1.3 shows that this analysis supports the curvilinear shape observed for most of the individual studies in Figure G1.2. The largest risk reduction is seen at the lowest end of the physical activity spectrum, and additional risk reductions — at smaller magnitudes — are seen at higher levels of physical activity. On average, it appears that compared to less than 0.5 hour per week of moderate-to-vigorous physical activity, engaging in approximately 1.5 hours per week of such activity is associated with about a 20% reduction in risk of all-cause mortality. Additional amounts of physical activity are associated with additional risk reductions, but at smaller magnitudes, such that an additional approximately 5.5 hours per week are required to observe a further 20% decline in risk (i.e., approximately 7.0 hours per week is associated with approximately 40% reduction in risk, compared with less than 0.5 hour per week).

Figure G1.2. Shape of the Dose-Response Curve: Relative Risks of All-Cause Mortality by Physical Activity Level (Studies With at Least 5 Levels of Physical Activity)

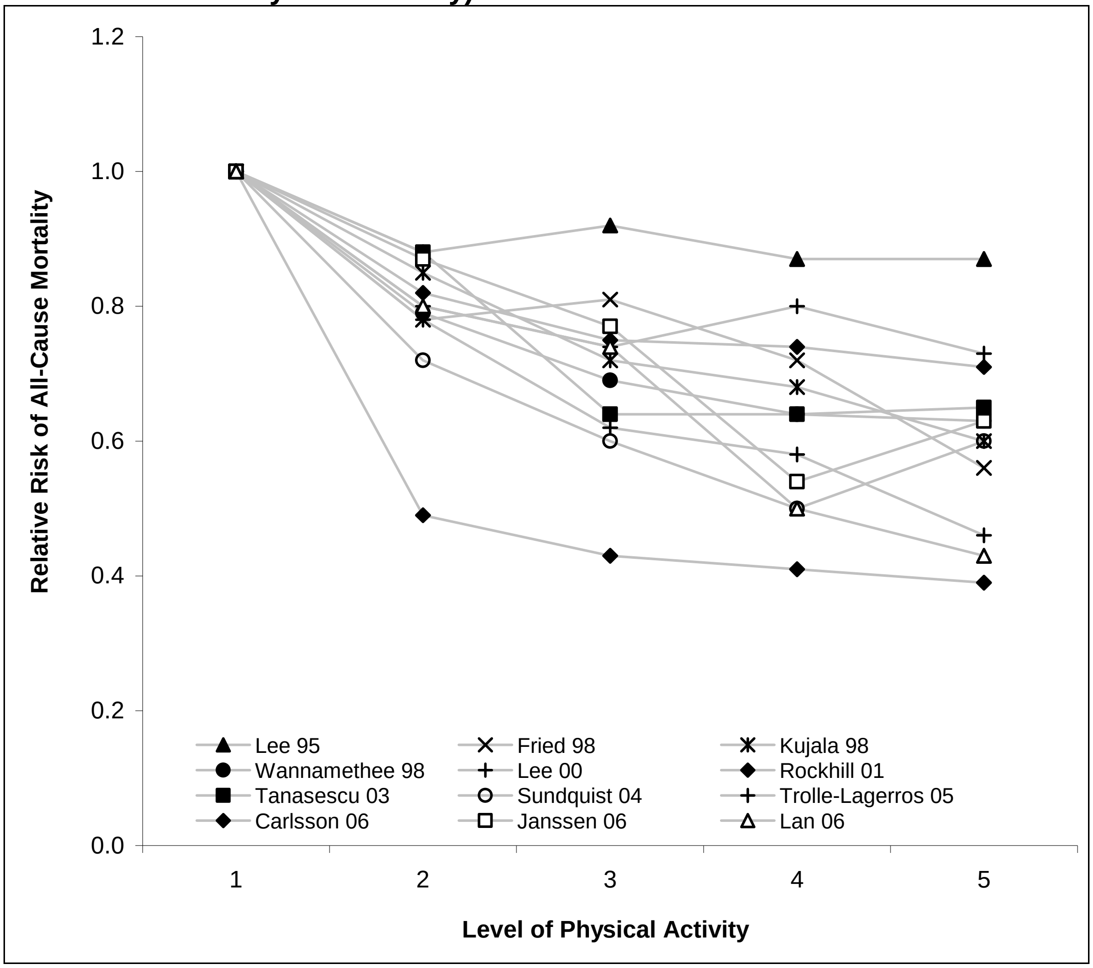


Figure G1.2. Data Points

Author/Year	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Lee 95	1	0.88	0.92	0.87	0.87	
Fried 98	1	0.78	0.81	0.72	0.56	
Kujala 98	1	0.85	0.72	0.68	0.6	
Wannamethee 98	1	0.79	0.69	0.64	0.63	0.54*
Lee 00	1	0.8	0.74	0.8	0.73	
Rockhill 01	1	0.82	0.75	0.74	0.71	
Tanasescu 03	1	0.88	0.64	0.64	0.65	
Sundquist 04	1	0.72	0.6	0.5	0.6	
Trolle-Lagerros 05	1	0.78	0.62	0.58	0.46	
Carlsson 06	1	0.49	0.43	0.41	0.39	
Janssen 06	1	0.87	0.77	0.54	0.63	
Lan 06	1	0.8	0.74	0.5	0.43	

*Not shown.

Figure G1.3. “Median” Shape of the Dose-Response Curve

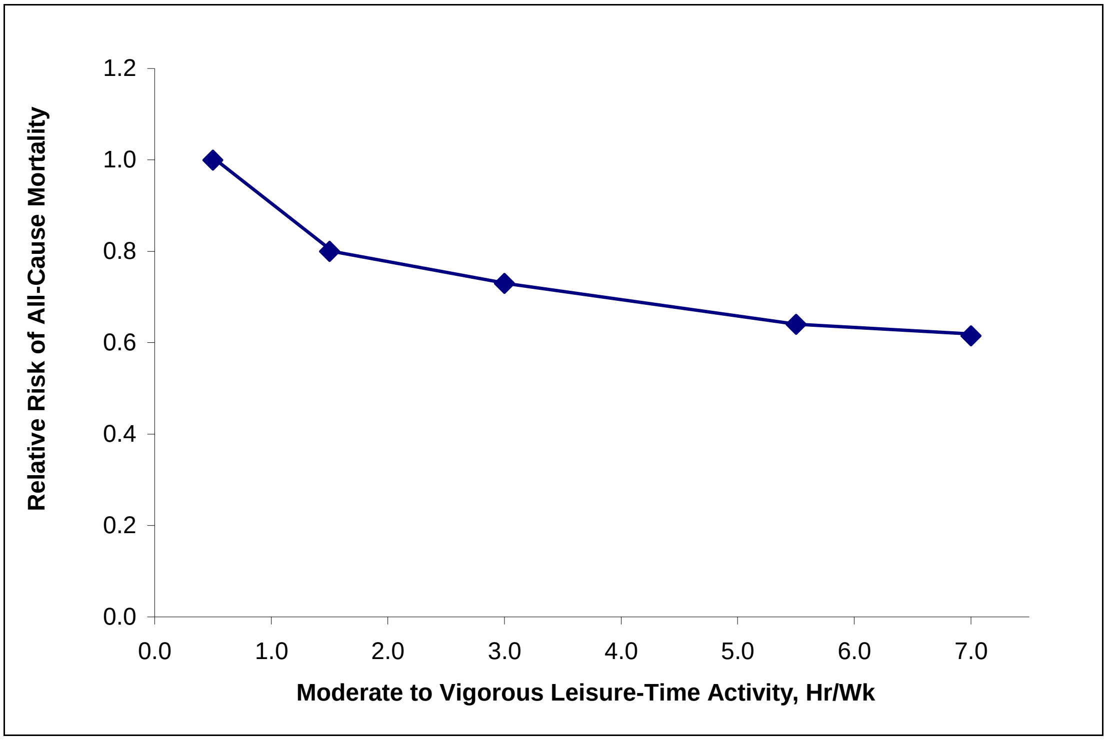


Figure G1.3. Data Points

Hr/wk	RR
0.5	1
1.5	0.8
3	0.73
5.5	0.64
7	0.615

Question 5: Is the Relation Between Physical Activity and All-Cause Mortality Independent of Adiposity?

Conclusions

The inverse relation between physical activity and all-cause mortality appears independent of adiposity. Further, this inverse relation appears to hold regardless of whether subjects are normal weight, overweight, or obese.

Rationale

Debate exists regarding whether adiposity should be adjusted for when examining the relation between physical activity and all-cause mortality rates. The argument against adjusting is that adiposity represents one pathway through which physical activity favorably influences mortality rates; thus, adjustment for adiposity minimizes the effect of physical activity. Nonetheless, almost 60% of the studies (43 of 73) adjusted their results for BMI or some other measure of adiposity (e.g., weight or waist-hip ratio). These studies, after adjustment for adiposity, continued to observe significant, inverse associations between physical activity and all-cause mortality.

Additionally, a few studies have stratified their findings by BMI, to examine the relation between physical activity and all-cause mortality among subjects with different BMI (3;11;31;54). These studies indicate that the inverse association between physical activity and all-cause mortality holds for persons who are normal weight, overweight, and obese. For example, among men in the Harvard Alumni Health Study (31), compared with inactive and **overweight** men, those who were active but overweight had a relative risk of 0.80 (95% CI, 0.71-0.91). Corresponding results were 0.90 (0.79-1.02) for men who were inactive but of **normal weight**, and 0.67 (0.60-0.75) for active and normal weight men. Among women in the Nurses' Health Study (3), using **normal weight**, active women as referent, normal weight women who were inactive had an elevated relative risk of dying during follow-up, 1.55 (1.42-1.70). Using the same referent, the relative risk for **overweight**, active women was 1.28 (1.12-1.46); for overweight, inactive women, this was 1.64 (1.46-1.83). For **obese**, active women, the relative risk was 1.91 (1.60-2.30); for obese and inactive women, this was 2.42 (2.14-2.73).

Overall Summary and Conclusions

The overall conclusions of this chapter on physical activity and all-cause mortality may be summarized as the following:

- A large body of scientific evidence, all from observational epidemiologic studies, exists on the association of physical activity with all-cause mortality rates.
- The data very consistently show an inverse relation, with the most active individuals — both men and women — experiencing approximately a 30% reduction in risk of mortality during follow-up, compared with the least active.
- The inverse relation extends to older persons, aged 65 years and older.
- Although this inverse relation has been observed in many countries throughout the world, the data that are specific to non-white populations are limited compared to those on white populations. The inverse relation appears to be similar for both white and non-white populations.

- Studies primarily have assessed leisure-time physical activity, including walking. There is, however, some evidence to indicate that it may be the overall **volume** of energy expended — regardless of which activities produce this energy expenditure — that is important to lower the risk of mortality.

- With regard to the minimum amount of physical activity needed, it appears that at least 2 to 2.5 hours per week of moderate-intensity physical activity are required to significantly lower all-cause mortality rates. Walking has been specifically investigated in several studies, and it also appears that walking at least 2 hours per week is associated with significantly lower all-cause mortality rates.

- However, this amount — 2 to 2.5 hours per week of moderate-intensity physical activity — does not represent a minimum threshold level for risk reduction. The data consistently support an inverse dose-response relation for the total volume of energy expended, which supports a "some is good; more is better" message. In particular, the data support a target of 2 to 2.5 hours per week of moderate-intensity physical activity for lowering all-cause mortality rates, and encourage any level of activity below this target for inactive groups of individuals.

- It appears that the shape of the dose-response curve is curvilinear (see Figure G1.2). On average across studies, compared to less than 0.5 hour per week of moderate-to-vigorous physical activity, engaging in approximately 1.5 hours per week of such activity is associated with about a 20% reduction in risk. Additional amounts of activity are associated with additional risk reductions, but at smaller magnitudes, such that another approximately 5.5 hours per week is required to observe a further 20% decline in risk (i.e., approximately 7.0 hours per week is associated with about a 40% reduction in risk, compared with the risk associated with less than 0.5 hour per week).

- Limited data support vigorous-intensity physical activity being associated with additional risk reduction, compared with lower intensity activities, beyond its contribution to the total volume of energy expended.

- No data are available to inform whether multiple, short bouts of physical activity versus a single, long bout that expends the same energy are differentially associated with all-cause mortality rates.

- Finally, the inverse relation between physical activity and all-cause mortality appears independent of adiposity. Importantly, this inverse relation appears to hold regardless of whether subjects are normal weight, overweight, or obese.

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Part G. Section 2: Cardiorespiratory Health

Introduction

Cardiovascular diseases (CVD) account for the majority of premature morbidity and mortality in the developed world. The influence of physical activity and the prevention and treatment of cardiovascular disease is therefore of great importance. In considering the effects of physical activity on cardiovascular health, one must address not only its influence on the development of symptomatic disease (e.g., heart attack and stroke) but also the influence on risk factors that are known to contribute to the development of symptomatic disease and are often indicative of sub-clinical asymptomatic vascular pathology. Most of the modifiable risk factors for cardiovascular diseases are metabolic in nature and are, in turn, modifiable by changes in physical activity. These metabolic risk factors include hypertension, atherogenic dyslipidemia, the axis of insulin resistance to metabolic syndrome to frank type 2 diabetes, and obesity. In turn, both physical inactivity and poor cardiorespiratory fitness are major risk factors for cardiovascular diseases.

Review of the Science

Overview of Questions Addressed

In this critical review of the knowledge base about the relations between cardiovascular disease and physical activity, cardiovascular disease should be construed to include coronary heart disease, cerebrovascular disease, and peripheral arterial disease. This section of the report reviews the data regarding this relation in two parts, sequentially addressing a series of questions about the presence and the nature of the relationship between physical activity and cardiorespiratory health. First, the section addresses the primarily observational data about physical activity and cardiovascular disease in separate sections dealing with coronary heart disease, cerebrovascular disease and stroke, and peripheral arterial disease. Then, using data from experimental studies, it explores the evidence of the relation between physical activity and several cardiovascular disease risk markers: hypertension, atherogenic dyslipidemia, vascular health and cardiorespiratory fitness. Influences of physical activity on insulin resistance, glucose control, metabolic syndrome and diabetes are addressed in ***Part G. Section 3: Metabolic Health*** and relations between physical activity and obesity are addressed in ***Part G. Section 4: Energy Balance***. Within each disease or risk factor category, this section reviews the supporting evidence and provides conclusions about the following 3 questions.

1. What is the nature of the relationship with physical activity?

2. What is known about the dose-response relationship with different characteristics of physical activity?

3. What is known about whether the effects of physical activity exposure can be obtained in smaller multiple bouts per day (accumulation) versus single daily bouts?

Data Sources and Process Used To Answer Questions

The Cardiorespiratory Subcommittee focused its review on studies performed since the publication of the *Surgeon General's Report on Physical Activity and Health* in 1996 (1), emphasizing disease prevention as opposed to disease treatment. The subcommittee drew heavily from the *Physical Activity Guidelines for Americans* Scientific Database (see ***Part F: Scientific Literature Search Methodology,*** for a detailed description of the Scientific Database). In addition, the subcommittee relied on expert knowledge of the authors to identify specific published studies that are critical for the knowledge base that may predate 1996, post-date the collation of the Scientific Database, or for outcomes that were not identified as part of the Scientific Database process (e.g., vascular health markers). Also, reviews in some subject areas (hypertension and atherogenic dyslipidemia) relied in part upon meta-analyses. Finally, for some topics (e.g., cardiorespiratory fitness), separate literature searches were performed in the PubMed database.

All of the prospective cohort and case-control studies included in this review provide self-report information on the habitual physical activity of the subjects, a standardized assessment of CVD clinical events and a comparison of event rates in subjects assigned to 2 or more categories of physical activity. For interventional experimental studies, the analysis was restricted to randomized controlled trials (RCTs) that had a sedentary (non physical activity intervention control arm or period) and studied at least 25 subjects per arm, unless the findings were highly significant with a lower number.

In general, the reviews and discussions address physical activity performed in the context of dedicated sessions of exercise. The assumption is that the specified exercise activity is performed in addition to and on top of normal physical activity performed as a part of activities of daily living. The data are primarily confined to dynamic aerobic (endurance) exercise, as the long-term cardiovascular prevention benefits of resistance and flexibility exercises are relatively little studied to date (2). An exception to this approach occurs when measures of total activity or occupational activity are use as exposure variables in prospective cohort or case-control studies.

Special Considerations and Limitations

The relation between dynamic aerobic exercise and cardiovascular health outcomes, including cardiorespiratory fitness is complex and can be thought of as a series of point estimates within a 3-dimensional matrix of continuous variables: exercise exposure, disease activity, and the magnitude of the response. The major limitation to exercise exposure recommendations for cardiovascular health outcomes is that any recommendation poorly conveys the concept that the location of any point estimate along each of these 3 axes is along a continuum of exposure and response, and should not be viewed as an absolute threshold below which no benefits accrue and above which benefits always accrue.

Continuum of Exercise Exposure

It is well accepted that aerobic exercise exposures can be characterized by an interaction between bout intensity, frequency, duration, and longevity of the program (3;4). The product of these characteristics can be thought of as volume and can be represented by the total energy expenditure (EE) of the exercise exposure. Exercise volume is referred to as the major focus of the exercise recommendation in some recent statements (5), thus allowing for the mixing of exercise bouts of varying intensity, frequency and duration. As recommendations are intended to be adopted for an individual's life-time, longevity is not considered here. However, it is clear that most benefits resulting from changes in physical activity and exercise patterns accrue over days, weeks, months and even years of exposure, and that the study and understanding of such time lines are of scientific and clinical interest and should be investigated further. Most of the data from experimental studies presented here regarding dose-response associations address the issue of varying intensities of exercise and do not control for bout duration, frequency, or total volume of the exercise exposure. In most observational studies, the major variable used as an exposure is activity amount (e.g., minutes, metabolic equivalent [MET]-minutes per day, miles per week) with the other exposure frequently being activity intensity. However, because total weekly EE usually is not controlled, it is possible that the effects of higher intensities observed in these studies might reflect the higher volumes performed, and that the volume of the activity exposure is the important operative. As will be apparent from the relation of exercise volume to the other variables, one cannot fix volume and also simultaneously study either intensity, frequency, or duration effects while controlling the other two. Relatively few interventional experimental studies examine exercise intensity while controlling for EE and even fewer study frequency or duration effects while controlling for EE. This makes the construction of a precise exercise dose for any given response problematic.

Continuum of Disease Progression

Cardiovascular disease is a continuum from asymptomatic fatty vascular streaks, to severe symptomatic coronary heart disease, to fatal myocardial necrosis and death. The same is true for cerebrovascular disease and stroke. The goal of this section is to focus primarily on primary cardiovascular disease prevention. As part of that process, we have explored some treatment effects on cardiovascular risk factors (e.g., atherogenic dyslipidemia and hypertension), the favorable modulation of which, by pharmacologic or lifestyle therapy, have been shown to be related to reductions in cardiovascular risk as well. The modulation of these risk markers may be the mechanism through which physical activity acts to reduce cardiovascular clinical events, as well. One should be aware that the activity exposure beneficial for primary cardiovascular health (the factors studied in this chapter) and prevention may or not apply to patients with clinically active and apparent cardiovascular disease, such as those in rehabilitation programs.

Role of Physical Inactivity in Disease Progression

A note about the importance of acknowledging the health risks of inactivity in studies of the effects of physical activity on cardiovascular risk factors is indicated here. In studies that include a sedentary inactive non-intervention control group for comparison to the exercise intervention groups, the inactive group consistently tends to demonstrate a worsening in health parameters over time. This is the health cost of physical inactivity, to be contrasted with the health benefits of regular physical activity. That is, the lack of physical activity in normal life leads to worsening in some parameters absent other life style changes, such as in diet. In some instances, the lack of worsening in some parameters over time demonstrated in intervention groups would appear to be an indication that the exercise or physical activity intervention has no effect, whereas, in fact, when compared to inactive control groups, a significant difference in response over time is observed.

Continuum of the Response

The response of biological parameters to dynamic aerobic exercise, and likely to resistance training as well, is a continuum from undetectable changes to highly significant, robust and clinical important ones that are highly dependent on the exercise exposure variables previously discussed. Consequently, it is likely that no given minimal intensity, frequency, duration or volume of exercise will result in a favorable response for any given outcome. Similarly, it is unlikely that any of these exercise variables has a level for **optimal** outcome. Furthermore, increases in exercise exposure do have tangible adverse outcomes that are primarily musculoskeletal and cardiovascular (see ***Part G. Section 10: Adverse Events***). Thus, potential increases in favorable outcomes of increasing exercise exposure must be balanced by the potential for increases in unfavorable outcomes.

Question 1: What Is the Relationship Between Physical Activity and Cardiovascular Morbidity and Mortality?

Conclusion

The results of recently published studies continue to support a strong inverse relation between the amount of habitual physical activity performed and CHD and CVD morbidity or mortality. For both men and women at middle age or older, remaining sedentary is a major independent risk factor, with persons reporting moderate amounts of activity having a 20% lower risk and those reporting activity of higher amounts or intensity having approximately a 30% lower risk than least active persons. These may be underestimates of the risk reductions (with the underestimate being on the order of 10%) because multivariate models in many studies include adjustments for hypertension, dyslipidemia, and glucose tolerance, conditions that may represent biological intermediates in the causal pathway. Although still limited, data also indicate habitual physical activity benefits the cardiovascular health of people of various races and ethnicities.

Introduction

Physical Activity and Health: A Report of the Surgeon General concluded by saying, “The epidemiologic literature supports an inverse association and a dose-response gradient between physical activity level or cardiorespiratory fitness and both CVD in general and CHD in particular. A smaller body of research supports similar findings for hypertension. The biological mechanisms for these effects are plausible and supported by a wealth of clinical and observational studies. It is unclear whether physical activity provides a protective role against stroke” (1, p.112). Since 1996, a large volume of research has been directed at better defining the relation between physical activity and various CVD clinical outcomes, the mechanisms by which the cardiovascular benefits of physical activity are likely mediated, and the characteristics of the dose of activity (type, intensity, frequency, session duration, and total volume) associated with lower CVD clinical event rates.

The following material provides an overview of the scientific literature since 1996 directed at establishing the effects of physical activity on various clinical cardiovascular outcomes and the issue of dose-response. The main focus is on the primary prevention of clinical events; therefore, most of the evidence comes from prospective cohort studies of at-risk populations. All of the studies included in this review provide self-report information on the habitual physical activity of the subjects, a standardized assessment of cardiovascular clinical events, and a comparison of event rates in subjects assigned to 2 or more categories of physical activity. These comparisons consisted of a measure of the relative risk (RR) for the groups and 95% confidence intervals for the measure of risk, including risk ratios, hazard ratios or odds ratios. In all the cited studies, the multivariate adjusted relative risks were recorded and used in any analysis. These adjustments varied from study to study but usually included at a minimum age, body mass index (BMI), cigarette smoking, blood pressure, and blood lipid concentrations. It is understood that using multivariate adjustments, which in some cases include measures of BMI, blood pressure, and blood lipids, could inappropriately decrease the magnitude of the relation between the physical activity exposure and the clinical outcome because some of the benefit of the activity might be mediated through these variables (“intermediate” or “mediator” variables). However, we considered this a more conservative approach than adjusting just for age and other selected demographic variables. In studies where RRs for more active versus the least active persons are presented using both limited adjustments and multivariate adjustments that accounted for potential “intermediate” variables, the RRs for limited adjustments show greater effects in the range of 10% (6-8). To determine whether a dose-response pattern existed between physical activity characteristics and the clinical outcome, data for at least 3 activity categories needed to be provided. The *Physical Activity Guidelines for Americans* Scientific Database was used to identify eligible studies published between January 1996 and June 2007. Also, selected studies that did not meet criteria for inclusion in the Database but provided ancillary data related to specific issues have been considered in this review, including meta-analyses and systematic reviews.

Rationale

Between January 1995 and June 2007, more than 60 studies were published that met the subcommittee's search criteria investigating the effects of habitual physical activity on cardiovascular morbidity and/or mortality in men and women throughout a wide age span and of various race and ethnicities. Much of the self-reported physical activity was performed during leisure time, but also included are data from occupational, household, and commuting activities. A majority of these data come from prospective cohort studies with the results from a limited number of case-control studies included. Studies tended to report outcomes for various clinical manifestations of *coronary heart disease* (e.g., fatal or nonfatal myocardial infarction, ischemic heart disease, cardiac death), a more general category of *cardiovascular disease* that could include a variety of manifestations of atherothrombotic vascular disease (e.g., coronary heart disease, stroke, other vascular disorders), and *stroke or cerebrovascular disease*. Data were organized from these studies by CHD, CVD, and stroke and then by sex with an emphasis on the magnitude of any relation and whether evidence of a dose response existed. The relation between a measure of physical activity and a CVD clinical outcome was considered significant if the 95% confidence interval did not include 1.0. A significant dose-response relation usually was based on P for trend being <0.05.

Coronary Heart Disease

The results of studies investigating the relation between habitual physical activity and CHD morbidity and/or mortality published since 1996 quite consistently show lower event rates in more physically active men and women than for their least active counterparts. Most notable has been the large increase in the number of studies that have included data on women, with 19 studies reporting data on women and 9 with data on men and women combined (see Table G2-1 for a summary of the studies and Table G2-A1 for selected data from individual studies) (Table G2-A1 can be accessed at http://www.health.gov/paguidelines/report/).

The studies of women reporting CHD clinical events included more than 200,000 subjects aged 20 to 85 years. For the prospective cohort studies, the median RR of having a CHD clinical event for women reporting participation in moderate intensity or amount of physical activity compared to women reporting no or only light intensity activity was 0.78, while the RR for women performing vigorous or high amounts of activity as compared to women eporting no or light activity was 0.62. These RRs are quite similar to those resulting from a

Table G2.1. Summary of Prospective Cohort Studies and Case-Control Studies Published in the English Language Since 1996 Reporting on the Relation Between Habitual Physical Activity and the Prevention of Coronary Heart Disease, Cardiovascular Disease, or Stroke

Data summaries for each study in this review are included in the Appendix.

Men

Condition Prevented	Prospective Cohort Studies Number of Studies Reporting RR	Prospective Cohort Studies Median RR M/L	Prospective Cohort Studies Median RR H/L	Prospective Cohort Studies Number of Studies Reporting D-R	Prospective Cohort Studies Number of Studies D-R Sig.	Case-Control Studies Number of Studies Reporting RR	Case-Control Studies Median RR M/L	Case-Control Studies Median RR H/L	Case-Control Studies Number of Studies Reporting D-R	Case-Control Studies Number of Studies D-R Sig.
Coronary Heart Disease	17	0.81	0.68	11	7	6	0.65	0.53	2	2
Cardiovascular Disease	10	0.78	0.70	3	2	1	0.65	0.67	0	0
Total Stroke	11	0.65	0.72	6	5	0	–	–	–	–

Women

Condition Prevented	Prospective Cohort Studies Number of Studies Reporting RR	Prospective Cohort Studies Median RR M/L	Prospective Cohort Studies Median RR H/L	Prospective Cohort Studies Number of Studies Reporting D-R	Prospective Cohort Studies Number of Studies D-R Sig.	Case-Control Studies Number of Studies Reporting RR	Case-Control Studies Median RR M/L	Case-Control Studies Median RR H/L	Case-Control Studies Number of Studies Reporting D-R	Case-Control Studies Number of Studies D-R Sig.
Coronary Heart Disease	13	0.78	0.62	8	5	6	0.62	0.44	3	1
Cardiovascular Disease	12	0.80	0.72	6	5	1	0.89	0.71	0	0
Total Stroke	8	0.82	0.72	5	4	0	–	–	–	–

Table G2.1. Summary of Prospective Cohort Studies and Case-Control Studies Published in the English Language Since 1996 Reporting on the Relation Between Habitual Physical Activity and the Prevention of Coronary Heart Disease, Cardiovascular Disease, or Stroke (continued)

Men and Women (Data Combined)

Condition Prevented	Prospective Cohort Studies Number of Studies Reporting RR	Prospective Cohort Studies Median RR M/L	Prospective Cohort Studies Median RR H/L	Prospective Cohort Studies Number of Studies Reporting D-R	Prospective Cohort Studies Number of Studies D-R Sig.	Case-Control Studies Number of Studies Reporting RR	Case-Control Studies Median RR M/L	Case-Control Studies Median RR H/L	Case-Control Studies Number of Studies Reporting D-R	Case-Control Studies Number of Studies D-R Sig.
Coronary Heart Disease	5	0.74	0.63	1	1	4	0.61	0.48	3	1
Cardiovascular Disease	5	0.87	0.72	2	1	0	–	–	–	–
Total Stroke	4	0.67	0.75	2	1	2	0.68	0.48	0	0

D-R, dose-response; H/L, high intensity or high amount vs. light intensity/amount; M/L, moderate intensity/amount vs. light intensity/amount; RR, relative risk (includes risk ratio, odds ratio or hazard ratio); Sig., significant.

meta-analysis of many of the same studies that were published between 1996 and 2003 (9). The conclusion from this meta-analysis for CHD was that physical activity was associated with a lower risk of CHD (as well as CVD and stroke) in a dose-response fashion with pooled RRs for both moderate amounts and high amounts being significant when compared to no or light activity. In the 6 case-control studies reported for women, the median RR was 0.62 for moderate versus no or light activity and 0.44 for vigorous intensity or high amounts of activity versus no or light activity.

Of the studies reporting on CHD in men, 16 were prospective cohort studies and 4 were case-control studies. Approximately 124,000 men aged 15 to 96 years at baseline were included as subjects. Most studies reported on leisure-time physical activity (LTPA) with a few studies including occupational activity, commuting, and sports participation. Among the prospective cohort studies, the median RR was 0.81 for moderate intensity or amount of activity versus no or light activity and 0.68 for vigorous intensity or high amounts versus light or no activity. For the 6 case-control studies, the median RR was 0.65 for moderate versus no or light activity and 0.53 for vigorous intensity or high amounts versus no or light activity. These values are of a similar magnitude to those reported in a systematic review of studies published between 1953 and 2000 (10) and in a meta-analysis published in 2001 that included data from studies published before and after the *Surgeon General's Report on Physical Activity and Health* (11). The lower CHD event rate for more active men was reported for both nonfatal and fatal CHD with no systematic difference in CHD incidence versus CHD mortality.

Five prospective cohort studies and 4 case-control studies were published in which the results for CHD events for men and women were combined. In the prospective cohort studies, the median RR was 0.74 for moderate intensity or amount versus no or light activity and 0.63 for high intensity or amount versus no or light activity. In the case-control studies, the RR was 0.61 for moderate activity versus no or light activity and 0.48 for high amounts or intensity versus no or light activity.

Cardiovascular Disease

In prospective cohort studies published since 1996 that included data on the relation between habitual physical activity and CVD in women (n=12), the median RR was 0.80 for those reporting moderate intensity or amount versus no or light activity and 0.72 for vigorous versus no or light activity. In the one case-control study reporting on CVD in women, the RR was 0.89 for moderate intensity versus no or light activity and 0.71 for high versus no or light activity. (See Table G2-A2 for selected data from these prospective cohort and case-control studies. This table can be accessed at http://www.health.gov/paguidelines/report/.) Here again, the amount and quality of data evaluating the relation between physical activity and CVD clinical events in women has substantially increased since 1996, with at least 350,000 women included in the reported studies. Overall, the CVD data reported on men are very similar to those for women: In 10 prospective cohort studies the median RR for CVD events was 0.78 for moderate versus no or light activity and 0.70 for high intensity or amount versus no or light activity. In the one case-control study, the RR was 0.65 for moderate versus light activity and 0.67 for high versus no or light activity. Although data are not provided in the reports, it is very likely that a majority of the CVD events included in these studies were the result of coronary heart disease.

Effects of Sex, Age, or Race and Ethnicity

Although the magnitude of median RRs for CHD for both moderate versus light activity and high versus light activity are somewhat lower in women than in men (Table G2-1), physically active men and women both typically have a lower risk for CHD than do their least active counterparts. Comparisons between the sexes are difficult across studies because of some evidence that the activity levels in the least active women are less than for the least active men, age distributions within age categories (e.g., 40 to 65 years, 65 to 79 years) are different from study to study, and CHD event rates within age categories differ between men and women. In the studies that included data for both men and women (12-20), even fewer presented results for men and women separately and in some studies that do, the number of CHD events in women is relatively small, thus substantially limiting the reliability of any analysis (19). In a case-control study published by Fransson and colleagues (20) evaluating the association between various types of physical activity and acute myocardial infarction, women appeared to be somewhat more protected than men. The RR for fatal and nonfatal MI in women comparing most active versus least active for total activity was 0.16 (95% CI 0.07-0.37), and the RR for the same comparison in men was 0.46 (95% CI 0.31-0.69). For women, the RR for LTPA more than 3 times per week versus seldom was 0.31 (95% CI 0.15-0.66); for men the RR was 0.53 (95% CI 0.38-0.73). It should be noted that rarely is a distinction made in these studies between associations in pre- and post-menopausal women, and whether they are different in these two populations when studied separately. Consequently, no evidence exists that effects of physical activity on CHD are different whether the study population is men, pre-menopausal, or post-menopausal women.

The inverse association between physical activity and CHD events has been reported for adults across a wide range of ages, with the magnitude of the association for older men and women (aged 65 years and older) at least as strong as for younger adults. Because CVD morbidity and mortality rates are low in men younger than age 45 years and women younger than age 55 years, very few data are available on the relation between physical activity levels and CVD clinical events in younger adults or youth. None of the meta-analyses on physical activity and CVD events published since 1995 has evaluated the effect of age on the magnitude of the relation, and only a limited number of studies have compared different age categories within their population. Manson and colleagues (21) had a sufficiently large sample of women (n=73,743) and cardiovascular events (n=1,551) in the Women's Health Initiative Observational Study to analyze the relation between LTPA and CVD incidence for 3 age groups, 50 to 59 years, 60 to 69 years, and 70 to 79 years. When activity was classified by MET-hours per week in quintiles, all 3 age groups showed a significant difference (*P* for trend <0.001) when the highest versus the lowest quintiles were compared (RR = 0.45, 0.50 and 0.64, respectively) with the lowest quintile being the reference (1.0) the adjusted RRs for quintiles 2 through 5 for women aged 50 to 59 years were 0.68, 0.63, 0.54, 0.45, respectively. For women aged 60 to 69, the RRs were 0.79, 0.63, 0.56, 0.50, respectively, and for women aged 70 to 79, they were 0.93, 0.86, 0.75, 0.64, respectively. Other studies have not showed any meaningful difference in the relation between physical activity level and CVD events in different age categories. For example, women in the College Alumni Health Study contrasting those younger than age 45 years versus those 45 years and older at baseline (22), combined data on men and women contrasting aged 65 years and younger versus those older than 65 years (23), or those aged 65 to 74 years versus aged 75 years and older (24). In a small prospective cohort study in men evaluating various risk factors for CHD, high-intensity activity was related to CHD events in those older than age 65 years (0.36, 95% CI 0.13-1.05) but not in those aged 65 years and younger (25). In the Buffalo Blood Pressure Study, older women (aged 60 years and older) were not protected from CVD mortality by high levels of total activity, though physical activity provided some protection for women younger than aged 60 years. However the number of CVD events was small in both groups (26).

Few studies conducted in the United States have had an adequate sample size and clinical outcomes to evaluate the association between physical activity and CVD clinical events in race or ethnic groups other than non-Hispanic whites. The Women's Health Initiative Observational Study (21) included 61,574 white women and 5,661 black women with a mean follow-up of 3.2 years. The relation between total physical activity level (quintiles of MET-hours per week) and CVD clinical events was significant for both groups of women with RR for the highest versus lowest quintile of activity for white women being 0.56 (P for trend <0.001) and for black women 0.48 (P for trend = 0.02). In contrast to these results, a report on the Atherosclerosis Risk in Communities (ARIC) study population indicated that although activity level and CVD clinical events had a significant inverse relation in white men and women, no such relation was found for either back men or women (19). The authors suggested that this lack of association in blacks may be due to the limited number of blacks reporting vigorous physical activity (5% in black men versus 15% in white men). However, outside the United States, where the relation between physical activity level and CVD clinical events has been evaluated in other race and ethnic populations, there is no indication that the favorable association frequently reported for non-Hispanic white men and women does not occur in other race and ethnic populations. For example, physically active Japanese men and women living in Japan (27) and older Japanese men living in Hawaii (28) had lower CVD mortality rates than the least active. Similar results have been reported for Chinese women living in Shanghai (29) and Chinese men and women living in Hong Kong (30). In a case-control study including men and women conducted in New Delhi and Bangalore India, at least 145 MET-minutes per day of LTPA versus no activity had a RR for myocardial infarction of 0.44 (95% CI 0.27-0.41). Time spent in non-work sedentary activity also was directly associated with risk of myocardial infarction (the RR for at least 215 minutes per day of sedentary activity versus fewer than 70 minutes per day was 1.58 [95% CI 1.05-2.36]).

Change in Physical Activity and Cardiovascular Disease Clinical Events

Most reports from prospective observational studies have presented the relation between physical activity measured on one occasion and the rate of CVD clinical events over various periods of follow-up. However, a few studies have obtained self-reported activity 2 or more times, typically 3 to 15 years apart, and related change in activity during this interval with CVD clinical events during a follow-up period. The goal of this approach is to determine whether an increase in activity is associated with lower event rates than observed for subjects who remain inactive. Also, do subjects who move from an active to an inactive category have higher CVD event rates than subjects who remain physically active? Men in the Harvard Alumni Study who increased their physical activity index to 2,000 kilocalories per week or more (measured in 1962 or 1964 and again in 1977) compared to men who remained inactive had a 17% lower CHD death rate (P= 0.51), while men who took up moderately vigorous sports had a 41% lower risk (P= 0.04) (31). Similar results have been reported for British men. Those who reported an increase in activity over 12 to 14 years had a RR for CVD mortality of 0.66 (95% CI 0.35-1.23) compared to men who remained sedentary, while men who remained active had a RR of 0.54 (95% CI 0.31-0.94) compared to continuously sedentary men (32).

Women in the Nurses' Health Study who reported increases in their LTPA between 1980 and 1986 with follow-up to 1994 had lower CVD event rates than women who remained sedentary (6). When the increase in activity for women who were sedentary in 1980 was expressed in quartiles of METs, the RRs for quartile 1 through quartile 4 were 0.85, 0.79, 0.67 and 0.71, respectively (P for trend=0.03). Women aged 65 years of age and older who had physical activity assessed twice (5.7 years apart) and changed from being inactive to active had a RR for CVD mortality of 0.64 (95% CI 0.42-0.97) compared to women who remained inactive, and women who remained active had a RR of 0.68 (95% CI 0.58-0.82). Although data on the association between change in activity and CVD clinical events in prospective observational studies does not provide the same level of evidence as data from RCTs, these results do add to the strength of the evidence linking higher levels of physical activity with lower CVD risk. In the studies cited, the change in activity preceded the clinical events and the direction of the association is consistent with an increase in activity causing a reduction in risk.

Question 2: What Are the Dose-Response Relations Between Physical Activity and Cardiovascular Morbidity and Mortality?

Conclusion

The inverse association between CVD clinical events and habitual physical activity exists across a wide range of types, amounts, and intensities of activity. People at highest risk are those who are least active and spend much of their day in activities that consume low amounts of energy. When compared to very sedentary persons, men and women who perform small amounts of moderate-intensity activity, such as 60 minutes per week of walking at a brisk pace, exhibit fewer CVD clinical events. People who perform more activity and/or at a faster pace are at an even lower risk, with much of the benefit derived when men and women are performing 150 or more minutes per week of moderate-intensity (3 to less than 6 METs) physical activity. Greater amounts of activity appear to provide greater benefit but the shapes of any dose-response relations have not been well defined. Vigorous-intensity activity (equal to or more than 6 METs) when performed for a similar duration as moderate-intensity activity results in greater energy expenditure and is associated with lower CVD event-rates. Much of the recent data are based on LTPA, but performing physical activity during an occupation, around the home, or while commuting all appear to provide benefit as well.

Rationale

In the studies reporting on CHD or CVD, the median RR difference for high levels of activity versus inactive or light activity categories was somewhat greater than the difference in the median RR for moderate levels of activity versus inactive or light activity, thus indicating a somewhat greater benefit from higher amounts or intensities of activity versus moderate intensity and amounts of activity. In the cohort studies that had 3 or more physical activity levels, authors frequently evaluated dose-response by calculating the linear trend and testing this trend for significance. If the *P* for trend was ≤0.05, then the dose response was considered significant. For CHD in women, 7 studies reported *P* values for dose response, and 3 of them were significant. Six studies reported dose response for CVD in women, with 5 reaching significance. For men, 7 of 11 studies reporting dose response for CHD were significant as were 2 of the 3 studies reporting on CVD. For studies that combined data on men and women, the one study that reported dose-response for CHD found it to be significant, and 1 of the 2 studies reporting on CVD was significant.

From a public health perspective, it is important to recognize that when the reference group in the population being studied is very sedentary, modest amounts of moderate intensity activity are associated with significantly reduced rates of CHD and CVD. For example, in 3 large prospective cohort studies of women in the United States (6;7;21), those who walked in the range of 1 to 2 hours per week versus non-walkers produced RRs for CVD or CHD events of 0.75 (95% CI 0.63-0.89; (21), 0.70 (95% CI 0.51-0.95; (6)), and 0.49 (95% CI 0.28-0.86; (7)) (Figure G2-1). The *P* for trend with multivariate adjustment for categories of walking amount (MET-minutes per week or duration (minutes per week) was significant (*P* <0.001) in all 3 studies. Also, walking at a faster pace was associated with a lower risk of CHD or CVD in these 3 studies, with those who walked at a pace 3.0 miles per hour and greater having a significantly lower RR than non-walkers (0.76, 0.70 and 0.52). The *P* for trend across walking pace was significant for all 3 studies. Other studies have reported on walking and CVD with either significantly lower RRs for men and women who walk regularly versus non-walkers (24) or favorable but non-significant trends for increased walking (22;28;33;34). There was no difference in a large study of Chinese women living in Shanghai where the least active reference group included walking from 0 to 3.4 MET-hours per week (29). In this study, the amount of walking in the reference group of Chinese women was sufficiently high that additional walking may not provided additional protection against CVD. Overall, these data on walking and CVD indicate that when brisk walking is performed 3 hours per week by otherwise sedentary persons, especially women, the CVD clinical event rate is significantly lower than for persons who do little walking or other physical activities.

Figure G2.1 Relative Risk of CVD in Women — Walking Amount/Week

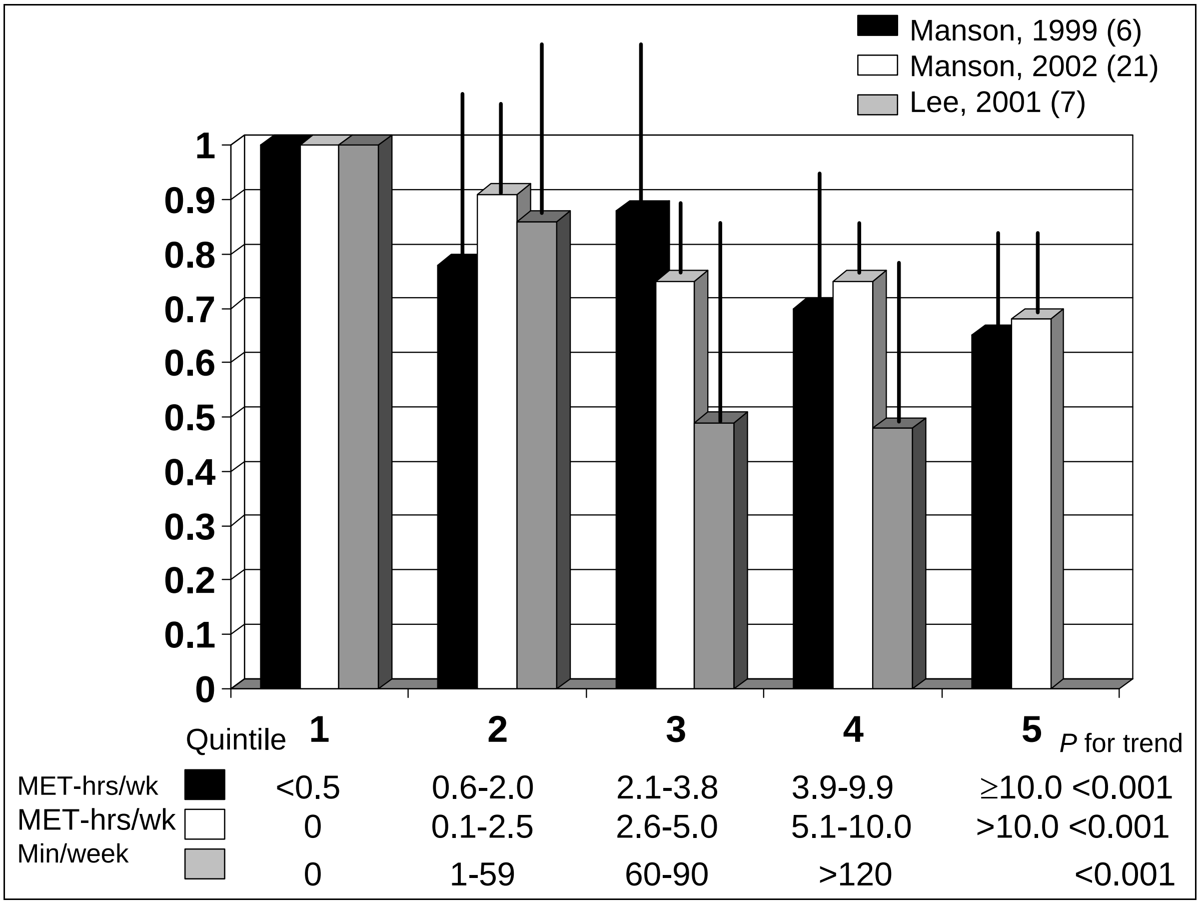

Figure G2.1. Data Points

Studies	1	2	3	4	5
Manson, 1999	1	0.78	0.88	0.7	0.65
Manson, 2002	1	0.91	0.75	0.75	0.68
Lee, 2001	1	0.86	0.49	0.48	

Question 3: What Is the Relationship Between Physical Activity and Cerebrovascular Disease and Stroke?

Conclusion

More physically active men and women generally have a lower risk of stroke incidence or mortality than the least active, with more active persons demonstrating a 25% to 30% lower risk for all strokes. A favorable relation exists between physical activity level and stroke (both for ischemic and for hemorrhagic stroke), but the data on these stroke subtypes are still quite limited. The benefits appear to be derived from a variety of activity types, including activity during leisure time, occupational activity, and walking. Overall, the relationship between activity and stroke is not influenced by sex or age, and very little data exist for race and ethnicity other than for non-Hispanic whites.

Rationale

The Surgeon General's Report on Physical Activity and Health concluded that "the existing data do not unequivocally support an association between physical activity and stroke risk" (1, p.103). This conclusion was based on a review of 14 observational studies (4 included women), of which 8 showed an inverse relationship between physical activity and stroke. The other studies showed no significant association, with 2 studies suggesting a U-shaped relationship with higher stroke risk in the least and most active categories. Since 1996, studies meeting the criteria for this review include data from studies on women (n=8), men (n=11), and men and women combined (n=6). (See Table G2-A3 for selected data from these prospective cohort and case-control studies. This table can be accessed at http://www.health.gov/paguidelines/report/.) In addition, 2 meta-analyses of physical activity and stroke have been published (35;36). In most studies, data are reported on all strokes, and in some studies data also are provided separately for ischemic and hemorrhagic stroke. In women, the median RR was 0.82 for all strokes combined for moderate-intensity activity versus no or light activity and 0.72 for high-intensity or amount versus no or light activity. For all strokes in men, the median RR was 0.65 for moderate-intensity versus no or light activity and 0.72 for high-intensity or amount versus no or light activity. In the studies reporting combined data on men and women, the median RR for the prospective cohort studies (n=4) was 0.67 for moderate-intensity versus no or light activity and 0.75 for high-intensity or amount versus no or light activity. For the 2 case-control studies, the median RR was 0.68 for moderate versus low activity and 0.48 for high versus low activity.

The meta-analysis by Wendel-Vos and colleagues (36) included data from 31 studies published in English before 2001, including 24 prospective cohort studies and 7 case-control studies. Based on these analyses, the authors concluded that moderately active men and women had lower rates of ischemic, hemorrhagic, and all strokes than did the least active subjects. When persons who reported moderate-intensity occupational activity were compared with persons who reported light-intensity occupational activity, the RR was 0.64 (95% CI 0.48-0.87). They also observed an RR of 0.85 (95% CI 0.78-0.93) for moderate versus light LTPA. High-level occupational activity appears to protect against ischemic stroke compared with both moderate (0.77, 95% CI 0.60-0.98) and inactive occupational levels (0.57, 95% CI 0.60-0.98). Persons reporting high-level compared to low-level LTPA were at significantly lower risk for all strokes (0.78, 95% CI 0.71-0.85), ischemic stroke (0.79, 95% CI 0.69-0.91), and hemorrhagic stroke (0.74, 95% CI 0.57-0.96). Both moderately active men and women had a lower RR for hemorrhagic stroke than their inactive counterparts (men = 0.54, 95% CI 0.36-0.81; women = 0.76, 95% CI 0.67-0.86; P=0.07 for difference between men and women). Studies conducted in Europe showed a stronger inverse association between active and inactive persons (0.47, 95% CI 0.33-0.66) compared to studies conducted in the United States (0.82, 95% CI 0.75-0.90). The overall results of the meta-analysis on physical activity and stroke published a year earlier (35) were similar to the results of this meta-analysis. When Lee and colleagues included data from both cohort and case-control studies, the RR for stroke incidence or mortality for the most active versus the least active was 0.73 (95% CI 0.67-0.79) and for moderately active versus the least active the RR was 0.80 (95% CI 0.74-0.86).

The inverse association between physical activity level and stroke risk appears very similar for men and women in the few studies that report sex-specific data. Vatten and colleagues (37) followed 34,868 Norwegian women and 32,872 men for 16 years and documented cause-specific mortality. The P for trend for total activity and stroke mortality was 0.009 for men and <0.001 for women, and the RR for high activity versus never active was significant for both sexes. In Japan, 31,023 men and 42,242 women were followed for an average of 9.7 years, and walking and sports participation were inversely related to CVD mortality (27). The relationship of walking time to all stroke or ischemic stroke mortality was very similar for men and women as was the time spent in sports participation. Because the occurrence of stroke is very low for those younger than age 55 years, very few reports are available on the relation of physical activity to stroke morbidity or mortality in younger and middle-aged populations. Data from the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study (38) indicate no systematic difference in the relationship of LTPA amount to either total or non-hemorrhagic stroke in men or women aged 45 to 64 years versus 65 to 74 years at baseline (the age x low activity interaction term was not significant). Overall, the strongest and most consistent association between activity level and stroke in this study was seen in white women.

Although stroke rates tend to be higher in African American men and women than in other race/ethnicities in the United States, no studies have adequately addressed the relation of physical activity level and stroke risk in any race/ethnicity other than non-Hispanic whites.

Question 4: What Is the Relationship Between Physical Activity and Peripheral Arterial Disease?

Conclusion

No large RCTs have been conducted to investigate exercise training in peripheral arterial disease (PAD). Little is known regarding exercise dose response (intensity, duration or frequency) or different modalities (walking, cycling, resistance training) of exercise to prevent PAD because most of the studies have followed the same exercise prescription, which has used supervised treadmill walking at a similar dose. Furthermore, even less is known about how subpopulations differ in responses to exercise training, such as whether sexes respond differently or whether an interaction exists between type 2 diabetes and exercise responsiveness in persons with PAD.

Rationale

Exercise for Primary Prevention of Peripheral Arterial Disease

Only a handful of cross-sectional primary prevention studies have been performed to relate ankle brachial index (ABI), an indicator of severity of peripheral lower extremity arterial occlusion, with physical activity (Table G2-A4, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.) Activity questionnaires have been used to examine retrospectively the relationship between physical activity and abnormal ABIs. In the Edinburgh Artery Study (39), for example, the amount of physical activity performed between the ages of 35 to 45 years was inversely related to prevalence of PAD at ages 55 to 74 years, but only in men. Further, this relation held only for men who had smoked at some time in the past. Gardner and colleagues (40) observed that the amount of physical activity was related to ABI measures in those without PAD, suggesting that regular habitual exercise may be related to the presence of sub-clinical asymptomatic PAD.

Exercise for Secondary Prevention of Peripheral Arterial Disease

Exercise training is a powerful secondary preventive measure for those with established PAD (Tables G2-A5 and G2-A6, which summarize these studies, can be accessed at http://www.health.gov/paguidelines/report/). Several meta-analyses and review articles summarize this body of literature (Table G2-A7, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/) (41-49). Although these studies unequivocally demonstrate exercise training to be beneficial for improving maximal walking ability, many lack necessary criteria such as large sample sizes, randomized and controlled designs, assessments of sex and dose-response effects, and differential responses in symptomatic (intermittent claudication) versus asymptomatic individuals needed to make strong specific clinical exercise recommendations. Despite these shortcomings, the data demonstrate that adherence to a structured supervised exercise program is currently regarded as the most effective treatment for symptomatic PAD. In all of the clinical studies noted above, the 2 most commonly measured variables used to determine the effectiveness of a

PAD therapy are peak walking time (PWT) and claudication onset time (COT). It is clear that exercise improves both PWT and COT in patients with PAD (50-64).

Based on the evaluation of meta-analyses and clinical studies, the average improvement following exercise training in PWT is near 100%, with COT improving consistently to an even greater degree (to the magnitude of 130% or more). Other responsive variables, primarily measured in small studies, are peak oxygen consumption, walking economy, daily physical activity, 6-minute walk time, leg blood flow, and quality of life. Interestingly, although some studies have demonstrated improved leg blood flow and ABI, these indices have not convincingly been related to functional markers. It appears that improved oxidative metabolism in the skeletal muscle may explain some of the improvements in exercise tolerance (50;52). Whether increased growth of small blood vessels (angiogenesis) and oxidative machinery (enzymes, mitochondria) are responsible for the improved muscle metabolism following exercise training is being explored. Findings also suggest that improvements can be augmented beyond those resulting from a traditional 12-week exercise program. As much as an additional 50% improvement in PWT may be achieved with continued therapy to up to 24 weeks (51). Twelve to 24 weeks of exercise training produced improvements in free-living accelerometer-derived daily physical activity, walking economy measured by constant workload oxygen consumption (slow component of VO_2). Although a traditional exercise prescription for PAD recommends that patients endure a moderate rather than severe level of claudication pain during training bouts, limited evidence indicates that a lower exercise intensity than the pain threshold elicits similar results as exercise above the pain threshold as long as the same dose in minutes is maintained (63).

The Relationship Between Daily Physical Activity and Peripheral Arterial Disease

Studies have confirmed that the severity of PAD is related to daily free-living physical activity. (Table G2-A8, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.) Studies show that, among individuals with PAD, daily physical activity is reduced approximately 40% compared to matched healthy controls and that the degree of claudication (as measured by ABI and PWT) is related to daily physical activity within a PAD population (65;66). These findings have been confirmed using accelerometers and performance score questionnaires that have related the decrease in daily physical activity to impairments in the lower extremity. A progressive decline in leisure-time activities of both moderate and high intensities has been identified in individuals with PAD (67). The loss of daily physical activity corresponds with decreasing ABI values and COT. Furthermore, a relation appears to exist between free-living physical activity and microcirculation in the calf muscle (66). The natural progression of PAD has been assessed and determined to be inversely related to self-reported physical activity as assessed by COT, 6-minute walk test, and calf blood flow (68). All of these studies demonstrate that, despite a lack of randomized controlled exercise studies to evaluate the effect of exercise training on preventing PAD, a lack of exercise contributes to disease progression, symptom status, and additional inactivity in those who have PAD.

Although most studies comparing supervised versus home-based programs conclude that supervised exercise is better, this remains inconclusive. No study has investigated the effects of an exercise program on asymptomatic patients with known PAD to determine whether exercise can prevent the onset of claudication or disease worsening. In addition, little is known about the role of resistance training, as no definitive trial has directly compared traditional walking exercise to resistance training in the PAD population.

Question 5: What Is the Relationship Between Physical Activity and Hypertension?

Conclusion

Both aerobic and progressive resistance exercise yield important reductions in systolic and diastolic blood pressure (BP) in adult humans, although the evidence for aerobic exercise is more convincing. Traditional aerobic training programs of 40 minutes of moderate- to high-intensity exercise training 3 to 5 times per week and that involve more than 800 MET-minutes of aerobic exercise per week appear to have reproducible effects on BP reduction.

Rationale

In this section we update the evidence of the effects of chronic exercise on resting BP in adults generated since the release of the *Surgeon General's Report on Physical Activity and Health* (1). This update is limited to a review of previous meta-analyses that met the following criteria: (1) RCTs only, (2) meta-analyses published in the English language between January 1, 1995 and September 30, 2007, (3) adults aged 18 years and older, (4) aerobic or progressive resistance training as the only intervention, (5) non-intervention control group, (6) resting or ambulatory systolic and diastolic BP as a primary outcome in each meta-analysis.

Relationship Between Aerobic Exercise and Blood Pressure

Ten meta-analyses dealing with the effects of aerobic exercise on resting BP in adults have been published since 1996 (69-78). Six of these meta-analyses were comprehensive (69;72;74-77) and the remaining 4 focused on either women (71), older adults (73), overweight and obese subjects (70), or walking as the only intervention (78). The most recent and inclusive meta-analysis that included data partitioned according to hypertensive, prehypertensive, and normotensive adults included a total of 72 studies, 105 exercise groups, and 3,936 men and women with a between-study age range of 21 to 83 years (median age = 47 years) (76). Across all categories, mean reductions in resting BP ranged from 2 to 5 mmHg (2% to 4%) for resting systolic BP and 2 to 3 mmHg (2% to 3%) for resting diastolic BP. Reductions were greater in hypertensive subjects (systolic BP, −6.9 mmHg; diastolic BP, −4.9 mmHg) than in prehypertensive (systolic BP, −3.1 mmHg; diastolic BP, −1.7 mmHg) and normotensive (systolic BP, −2.4 mmHg; diastolic BP, −1.6 mmHg) subjects. Changes were equivalent to relative reductions of approximately 5% for both resting systolic and diastolic BP in hypertensive subjects, 1% (systolic BP) and 2% (diastolic BP) in prehypertensive subjects, and 2% for both resting systolic and diastolic BP in normotensive subjects. Significant reductions of 3.3 mmHg (2%) and 3.5 mmHg (4%) also were observed for daytime ambulatory systolic and diastolic BP with no significant change in nighttime BP. Changes in ambulatory BP are especially noteworthy because the assessment of the measure may better predict target end-organ damage (79). Changes in both resting and ambulatory BP were independent of changes in body weight (76). Similar changes in resting BP also were found for the other inclusive meta-analyses (69;72;74-77) as well as meta-analyses that focused on women (71), older adults (73), overweight and obese subjects (70), and walking (78).

Dose-Response Relations Between Aerobic Exercise and Blood Pressure

The vast majority of studies included in the meta-analyses conducted since the release of the *Surgeon General's Report on Physical Activity and Health* (1) have tended to follow traditional guidelines for the prescription of aerobic exercise in adults as recommended by the American College of Sports Medicine (5;80;81). For example, for the most recently published meta-analysis dealing with the effects of aerobic exercise on resting BP (77), the pooled median length of training was 16 weeks, with a frequency of 3 days per week. However, the analysis included studies in which subjects exercised up to 7 days per week, with a duration of 40 minutes per session and intensity of 65% of maximal heart rate reserve. No consistent relations were observed between changes in resting systolic and diastolic BP and the length, frequency, duration, and intensity of training (77). The most common forms of exercise used in these RCTs were walking, jogging, and stationary cycling, although other types of exercise, such as aerobic dance, also were included. Other meta-analyses also have failed to find a relation between training program characteristics and changes in resting BP (69-72;74-76;78). In contrast, one meta-analysis did report larger decreases in resting systolic and diastolic BP with a greater duration (minutes) of training per session as well as greater decreases in resting systolic BP with lower training intensities (73).

Relation Between Progressive Resistance Exercise and Blood Pressure

Since the release of the *Surgeon General's Report on Physical Activity and Health* (1), 3 meta-analyses (45;77;82) have been conducted on the effects of progressive resistance exercise on resting systolic and diastolic BP. However, as 2 of these included the same data (77;82), this discussion is limited to the one that contained more complete data on progressive resistance training (82). This meta-analysis included 9 RCTs and 12 exercise groups comprising 341 men and women aged 20 to 72 years (median age = 69 years). The vast majority of subjects were not hypertensive (baseline resting systolic/diastolic BP values, 131.6/80.9 mmHg) (82). With the one static (isometric) training study deleted from the analysis, a statistically significant reduction of 3.1 mmHg was found for resting diastolic BP with a trend for a reduction in systolic BP of 3.1 mmHg. Similar and statistically significant reductions of 2% and 4% also were found for resting systolic and diastolic BP in an earlier meta-analysis that excluded static training studies (45).

Progressive Resistance Exercise and Blood Pressure

For the most recent meta-analysis (82) progressive resistance training took place over a mean duration of 16.4 weeks, 2 to 3 days per week at 61% of one-repetition maximum. The mean number of exercises was 10 while the number of sets was 2. Omitting the static study, the number of repetitions ranged from 8 to 25. Ten of the 12 groups (83%) used exercises that involved both the upper and lower body. Three of the 9 studies in the meta-analysis used a circuit training protocol, one used a static protocol, and the remainder used more conventional types of training protocols. No differences in resting systolic and diastolic BP were found between traditional and circuit training protocols.

Significance of Exercise-Induced Reductions in Blood Pressure

Although the reductions in BP as a result of aerobic and progressive resistance training may appear to be small, especially for normotensive and prehypertensive groups, they are clinically significant. It has been estimated that as little as a 2 mmHg reduction in population average resting systolic BP can reduce mortality from coronary heart disease, stroke, and all causes by 4%, 6% and 3%, respectively, while a reduction of 5 mmHg can reduce mortality risk by 9%, 14%, and 7% (83). The potential numbers of annual lives saved in the United States as a result of these reductions has been estimated at 11,800 for a 2 mmHg reduction in resting systolic BP and 27,600 for a 5 mmHg reduction (83).

Question 6. What Is the Relationship Between Physical Activity and Atherogenic Dyslipidemia?

Conclusion

For the purposes of this review, atherogenic dyslipidemia is defined as the presence of abnormally low serum concentrations of high-density lipoprotein (HDL) cholesterol and elevated concentrations of high triglycerides (TG) and small, dense low-density lipoprotein (LDL) cholesterol. The response of serum lipoproteins to changes in habitual physical activity have been well studied. In general, both HDL cholesterol and serum TG reproducibly and favorably respond to changes in habitual physical activity, with increases in HDL cholesterol and decreases in serum TG, mostly related to the volume of exercise training and responding with threshold volumes in the range of 7 to 15 miles per week of regular exercise (equating to an approximate 600 to 800 MET-minutes). Some evidence indicates that women are less responsive than men to change in habitual exercise, perhaps due to the observation that those with the largest baseline abnormalities (lower HDL and higher TG) gain the greatest benefit and men on average have lower HDL and higher TG than do women. However, when weekly volume or energy expenditure is controlled for men and women, the sex-related differences seem to be mitigated. Some inconsistent evidence suggests that LDL cholesterol may respond favorably to exercise training under some conditions; when it does, it is at the same volume thresholds as observed for HDL and TG. Finally, more recent studies have observed that fractionated serum lipoproteins respond favorably to aerobic exercise training in a dose-response fashion that is related to the weekly volume of exercise.

Rationale

A large volume of information is available on the exercise responsiveness of serum lipoproteins and dose-response effects, much of it accumulated before the 1996 *Surgeon General's Report*. For this review of the literature regarding the relation between habitual exercise and serum lipoproteins, we have relied mostly upon meta-analyses and reviews assembled since 1996. The relevant information is well summarized in 2 relatively recent reviews from Durstine and colleagues (84) and Leon and Sanchez (85). Most of the information before 1996 is based upon responses in total cholesterol and fractionated lipids (i.e., HDL, LDL, and TG). Recently some new information has emerged on the response of lipoprotein sub-fractions to exercise training (86;87).

The response of HDL cholesterol to exercise training traditionally has been well studied. As illustrated in a recent meta-analysis of exercise-induced effects on HDL cholesterol (88), the volume of exercise exposure is the primary determinant of exercise-induced modulations of HDL at a EE threshold of 10 to 12 MET-hours per week. Thus, although some evidence exists that exercise intensity may be related to HDL increasing as a result of exercise, this effect becomes insignificant when total exercise volume is controlled.

Women seem to be more resistant to modulation of TG through exercise interventions than are men, although this is not a consistent finding. In some studies, TG appear to be more responsive to lower volumes of exercise training than the volumes to which HDL is responsive, mimicking the responses in insulin action to which TG levels are closely tied (87). However, the sum of the literature seems to indicate that triglycerides are consistently, reproducibly and robustly responsive to exercise training of volumes that are comparable to those that induce changes in HDL (10 to 20 MET-hours per week) and that moderate-intensity exercise results in more sustained changes in TG than does high-intensity exercise once the training stimulus is removed (87).

LDL cholesterol is generally found not to be responsive to exercise training interventions. However, in the few circumstances when LDL has been observed to be modulated by exercise, it requires approximately 12 MET-hours per week of exercise to favorably influence LDL. Recently, studies of the modulation of fractionated lipoproteins with exercise training have shown that HDL, TG, and LDL size and number are favorably modulated in a dose-response fashion to exercise training related to training volume and that 800 MET-minutes of exercise per week was required for an effect different from that of a sedentary control group, whose LDL parameters tended to worsen over time in the absence of other lifestyle changes (87). More work is needed to understand the magnitude, consistency, and mechanism of these effects.

Question 7: What Is the Relationship Between Physical Activity and Vascular Health?

Conclusion

Habitual aerobic exercise appears to induce favorable responses in measures of vascular health. Exercise training initially increases brachial artery flow-mediated dilation (BAFMD—a measure of endothelial vascular health) with later normalization of BAFMD as vessels become structurally larger. Habitual aerobic exercise appears to slow the progression of age-related central arterial stiffening in healthy subjects. Increased levels of habitual physical activity are associated with slowed progression of carotid intimal medial thickening (CIMT) in cross-sectional and prospective cohort studies. No significant dose-response data are available for any of these measures.

Rationale

This section summarizes the effects of chronic aerobic exercise training on measures of vascular health, including BAFMD, arterial stiffness, and CIMT.

Brachial Artery Flow-Mediated Dilation

Dysfunction of endothelial cells is an early event in the process of atherosclerosis (89), and is associated with risk factors for cardiovascular disease (90-92). These relations have led to the use of endothelium-mediated vascular responsiveness as a surrogate biomarker of vascular health. Brachial artery flow-mediated dilation, a non-invasive measure of endothelial function, has been shown to correlate with measures of coronary artery function (93;94) and independently predicts cardiovascular events in patients with established disease (95-100). Due to its non-invasive nature and relative ease of use, BAFMD has become increasingly used as a research tool to monitor the efficacy of interventions on vascular health.

This section provides a review of the current published data on the effects of exercise training as the primary intervention on BAFMD. A total of 300 abstracts were initially retrieved and reduced to 22 separate intervention groups (57;99;101-119). All data included were from RCTs with a minimum exercise training intervention of at least 1 week and BAFMD data reported at both pre- and post-exercise training. Studies include data from both apparently healthy subjects as well as those with chronic heart failure, obesity, dyslipidemia, coronary heart disease, metabolic syndrome, uncomplicated myocardial infarction, heart transplant, and diabetes.

The results from this literature review provide convincing evidence that exercise training produces significant changes in the vascular health biomarker BAFMD. Figure G2-2 graphically illustrates the effect sizes seen in all intervention groups. Fifteen of the

Figure G2.2. Effect Sizes Seen in Interventions in Which BAFMD Is Used as a Vascular Health Biomarker

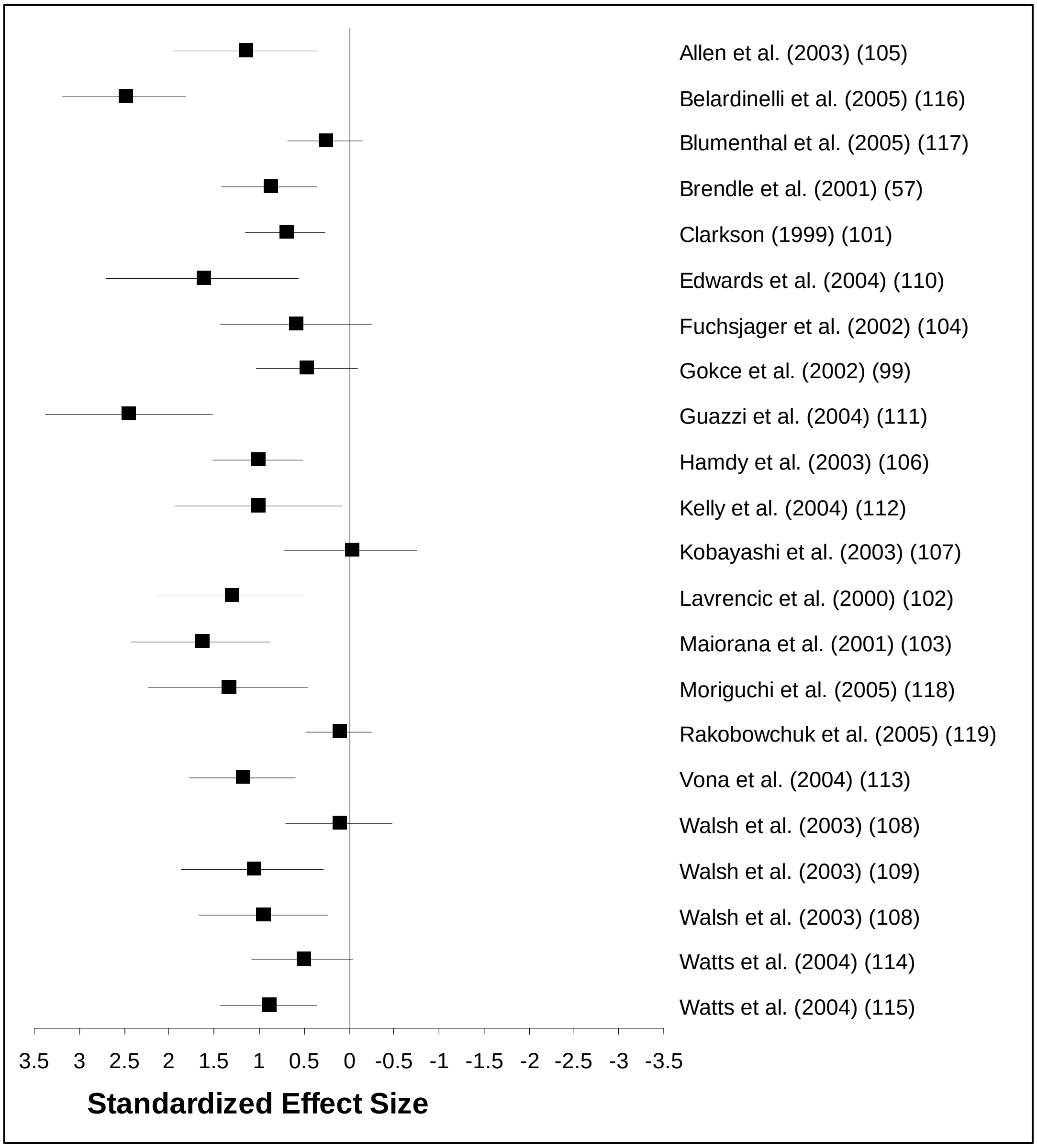

Figure developed from Clark O; Djulbegovic B. Forest plots in Excel software (data sheet). 2001. Available at www.evidencias.com.

Figure G2.2. Data Points

Upper Limit of the Confidance Interval	Lower Limit of the Confidance Interval	Point Estimate	Studies
1.96	0.36	1.16	Allen et al. (2003) (105)
3.18	1.82	2.5	Belardinelli et al. (2005) (116)
0.69	-0.14	0.27	Blumenthal et al. (2005) (117)
1.42	0.35	0.88	Brendle et al. (2001) (57)
1.15	0.27	0.71	Clarkson (1999) (101)
2.7	0.56	1.63	Edwards et al. (2004) (110)
1.44	-0.25	0.6	Fuchsjager et al. (2002) (104)
1.04	-0.09	0.47	Gokce et al. (2002) (99)
3.38	1.52	2.45	Guazzi et al. (2004) (111)
1.52	0.52	1.02	Hamdy et al. (2003) (106)
1.94	0.08	1.01	Kelly et al. (2004) (112)
0.72	-0.76	-0.02	Kobayashi et al. (2003) (107)
2.12	0.51	1.31	Lavrencic et al. (2000) (102)
2.42	0.88	1.65	Maiorana et al. (2001) (103)
2.23	0.46	1.35	Moriguchi et al. (2005) (118)
0.48	-0.26	0.11	Rakobowchuk et al. (2005) (119)
1.78	0.6	1.19	Vona et al. (2004) (113)
0.71	-0.47	0.12	Walsh et al. (2003) (108)
1.86	0.28	1.07	Walsh et al. (2003) (109)
1.68	0.23	0.96	Walsh et al. (2003) (108)
1.08	-0.04	0.52	Watts et al. (2004) (114)
1.43	0.36	0.89	Watts et al. (2004) (115)

22 intervention groups included in the analysis showed a statistically significant improvement in BAFMD (confidence intervals did not contain zero) in response to exercise training. Of the remaining 7 studies, only one produced a negative effect size (107).

Several factors modulate the magnitude of exercise-induced responses in BAFMD. The most influential of these appears to be health status before the exercise training intervention. That is, the magnitude of BAFMD improvement following training is, in part, a function of the initial or pre-training level. Subjects with cardiovascular disease exhibit greater improvements in BAFMD following exercise training but start with a lower pre-training BAFMD. Apparently healthy subjects also show improvement in BAFMD but not to the same degree as those with cardiovascular disease. The data on apparently healthy subjects come from only 3 studies and so should be interpreted with some caution (101;105;119). Interestingly, age does not appear to influence the magnitude of BAFMD response, suggesting it is modifiable in both young and old.

A second important moderator of response is the type of exercise performed. Changes in BAFMD were noted in most studies regardless of modality. However, the greatest affect was seen in those studies using aerobic exercise alone (14 studies) or in combination with resistance training (6 studies). The evidence for resistance training alone (2 studies) are less convincing, suggesting resistance training by itself may not be as effective in improving BAFMD.

A third moderator of response is length of the training period. Shorter periods of exercise training (8 weeks or less) result in larger changes in BAFMD compared to longer periods of training (more than 8 weeks). This implies that changes in BAFMD occur rapidly after initiating training but may diminish with time. This is consistent with the theory that vascular responses to aerobic exercise training consist of a series of stress-response-adaptation responses, where exercise is the stressor, increased BAFMD is the initial response, and structural vessel enlargement is the eventual adaptation (with subsequent normalization of the BAFMD response) (120).

As noted, the modality-specific (aerobic versus resistance) exercise training responses requires further study. Similarly, the dose-response effects of aerobic exercise training are notably understudied.

Carotid Intimal-Medial Thickening

Most studies on this outcome are prospective or case-control observational studies. Relatively few studies have examined the effects of exercise training on CIMT or progression. From 7 available cross-sectional studies, 4 report lower CIMT in subjects with higher physical activity levels (121;122) or higher VO_{2peak} (123;124). The remaining 3 studies found no difference between active and sedentary groups (125-127). The discrepancies between these study results could be related to differences in age and health of participants, methods of activity measurement and reporting, concomitant lifestyle changes, length of measurement, and differences in the techniques used to quantify CIMT.

The results from interventional studies make it even more difficult to draw definitive conclusions. From 8 available studies (127-134), only 3 appear to have reported the effects of exercise training isolated from other concurrent treatments (127;130;132) and none of these showed significant effects (135). Unfortunately, 2 of these studies were underpowered to detect CIMT progression, and the third was a pharmaceutical trial where exercise served as a control and no changes were observed after 4 years (132).

A lack of adequately powered exercise interventional studies is understandable if one considers the small size of the pooled annual rates of changes in CIMT progression that occur among control groups from randomized placebo-controlled trials. For studies using multiple IMT measures from several interrogation angles and carotid segments, the mean maximum progression rate was 0.0176 millimeters per year with a median SD of 0.05 (136). Given that sample size calculations rely heavily on rates of change, precision of the measurement, and projected effectiveness of the intervention, the subject numbers required and length of exercise training assessment period would have to be much longer than is traditional in such studies. For example, for a 30% treatment effect, average change in mean-max CIMT of 0.0352 ± 0.05 millimeters over 2 years, and using as two-tailed alpha, one would need 468 subjects in each arm of the trial to have 90% power.

Arterial Stiffness

Central arterial stiffening occurs with aging (137) but is often both a consequence and mechanism of atherosclerotic vasculopathy. The investigation of arterial stiffness has increased in recent years due to the development of noninvasive assessment techniques (138-140). However, there appears to be a lack of consensus regarding the most accurate and reliable method to measure arterial stiffness, complicating the determination of the efficacy of exercise training responses. The most frequently reported assessment methodologies are pulse wave velocity, pulse wave analysis, and distensibility/compliance (change in diameter/change in pressure).

Using these outcome measures, habitual aerobic exercise appears to slow the progression of age-related central arterial stiffening in healthy subjects as reported in several cross-sectional studies (137;141-143). Furthermore, 4 training intervention studies report significant improvements in measures of central stiffness across sex and age ranges (141-144). Interestingly, the benefits in central elastic arteries were not replicated in peripheral muscular arteries (142;145), suggesting that training-specific responses, or different mechanisms are active in different arterial beds.

The benefits of short-term aerobic exercise training on central stiffness in patient populations are less clear. One study reported a decrease in aortic pulse wave reflection in chronic hemodialysis patients following 3 months of aerobic training. This measure returned to pre-training levels 1 month after training ceased (detraining) (146). Another showed favorable changes in coronary artery disease subjects within 12 weeks (110), although other studies reported no effects of training in hypertensive (147;148) or diabetic (149) subjects.

Finally, the effects of resistance training on central arterial stiffness are conflicting. Two cross-sectional studies report a decrease in central but not peripheral arterial compliance in comparison to sedentary controls (143;150). In contrast, of 4 available case controlled interventional studies, 2 report increases in measures of central arterial stiffness (151;152) and 2 report no significant effect (153;154). These differences appear to be related to intensity, with higher training intensities eliciting higher central stiffness values. Clearly, large-scale prospective studies are warranted to clarify these discrepancies and to further elucidate the possible mechanisms involved in the observed changes.

Question 8: What Is the Relationship Between Physical Activity and Cardiorespiratory Fitness?

Conclusion

Cardiorespiratory fitness is a sensitive and useful measure of changes in response to physical activity. It demonstrates dose-response relations with overall exercise volume and also with each of the various components of exercise volume (intensity, frequency, duration, and longevity). It appears that one can acquire improvements in cardiorespiratory fitness in bouts as small as 10 minutes each, while holding volume constant. It is unclear whether there is a relation between the duration of exercise bouts and fitness responses, when total volume is held constant, especially for vigorous intensity exercise. Changes in fitness during exercise interventions correspond with changes in cardiovascular risk, but do not always correspond with changes in cardiovascular risk factors.

Rationale

Cardiorespiratory fitness, as measured by a number of relatively simple and inexpensive clinical maneuvers, provides strong and independent prognostic information about overall morbidity and mortality. This relationship extends to men, women, and adolescents. It is valid in apparently healthy individuals; in patients with a broad range of maladies, including several types of cancer and cardiovascular disease; and in at-risk individuals with type 2 diabetes, metabolic syndrome, and hypertension (1;155;156). Fitness is also a marker for functional capacity and ability to perform activities of daily living, especially in older individuals. Finally, it is used as an outcome measure of adherence and physical activity exposure in intervention studies. For example, men who improve their fitness (as assessed by exercise duration) improve their cardiovascular risk. In one report, long-term cardiovascular risk decreased by 8% for every minute increase in exercise capacity (157). Due to the correlation between fitness and health status, the responsiveness to changes in physical activity, and its usefulness as a marker of physical activity levels, cardiorespiratory fitness is an important health outcome measure in and of itself and is often quoted as an outcome in health-related physical activity studies. That said, favorable changes in fitness do not always correspond to change in health outcomes in response to exercise recommendations (158). The data for this section was acquired from an independent literature search of the PubMed database using “cardiorespiratory fitness” as a search term and identifying meta-analyses and review articles from both the 1996 date to the present and before 1996.

Cardiovascular fitness, as measured by any one of a number of parameters associated with exercise testing (peak VO_2, resting heart rate, lactate level or heart rate at submaximal exercise level, VO_2 at ventilatory threshold, time to exhaustion, and others) is extremely sensitive to changes in physical activity levels and habitual exercise. This is often referred to as a training effect. The training effect shows a strong dose-response relation to changes in exercise pattern of various types. Changes in fitness are dependent upon the frequency, duration, and intensity of exercise bouts and are also dependent upon the longevity of the exercise training program or intervention (reviewed in 3). The product of exercise frequency, bout duration, and intensity over time is often referred to as exercise volume and is proportional to exercise-related energy expenditure. A rich literature exists about the specific relation between the characteristics of exercise exposure and changes in cardiorespiratory fitness in the short and long term (3;4;159;160) in individuals of all ages, including older men and women (161-163). An example of the changes in cardiorespiratory fitness with training programs of various intensities and amounts (volumes) is demonstrated in Figure G2-3 (164). As shown, effects on cardiorespiratory fitness of exercise occur both with increasing intensity at the same volume, and increasing volume at the same intensity. The groups are clearly distinguishable by differences in group mean differences over time. However, it is also clear that baseline fitness and the ability to respond to an exercise intervention have numerous inputs other than physical activity pattern, one of which is genetic (165). Using the same study population as in the previous figure, when individual responses to training stimuli are displayed as individual data points ordered by magnitude of response, it is apparent that the identical stimulus can result in a broad range of responses, from negative to positive (Figure G2-4). That is, even a strong stimulus (high-volume, high-intensity exercise) can result in no significant improvement or even deterioration in cardiorespiratory fitness in some individuals, while resulting in a large magnitude of change, much larger than the group mean, in others. This observation has implications for the construction of physical activity recommendations, depending on whether the goal is to significantly move the population mean (e.g., 50%) or to affect a significant response in the vast majority of individuals, in which case a more robust exposure may be required.

As previously noted, changes in cardiorespiratory fitness in response to an exercise intervention depend upon a number of parameters, including the characteristics of the exercise stimulus, baseline fitness, sex, age, body mass index, and others. In addition, health benefits that accrue with an exercise program are often, but not always, correlated with changes in fitness (160). Two recent studies illustrate the dose-response relations between exercise exposure and fitness, as well as to several seminal cardiovascular risk markers. The results from the DREW (166) and STRRIDE (158;164) studies are summarized in Table G2-2. Cardiorespiratory fitness (peak VO_2) can be expressed in absolute terms (liters of oxygen consumption per minute) or relative to body mass (ml/kg/min). Exercise exposure in volume can be expressed as energy expenditure or as multiples of resting oxygen consumption (METs), times duration (e.g., MET-hour), where 1 MET approximately equals 3.5 ml/kg/min).

Figure G2.3. Changes in Peak VO_2 by Exercise Group

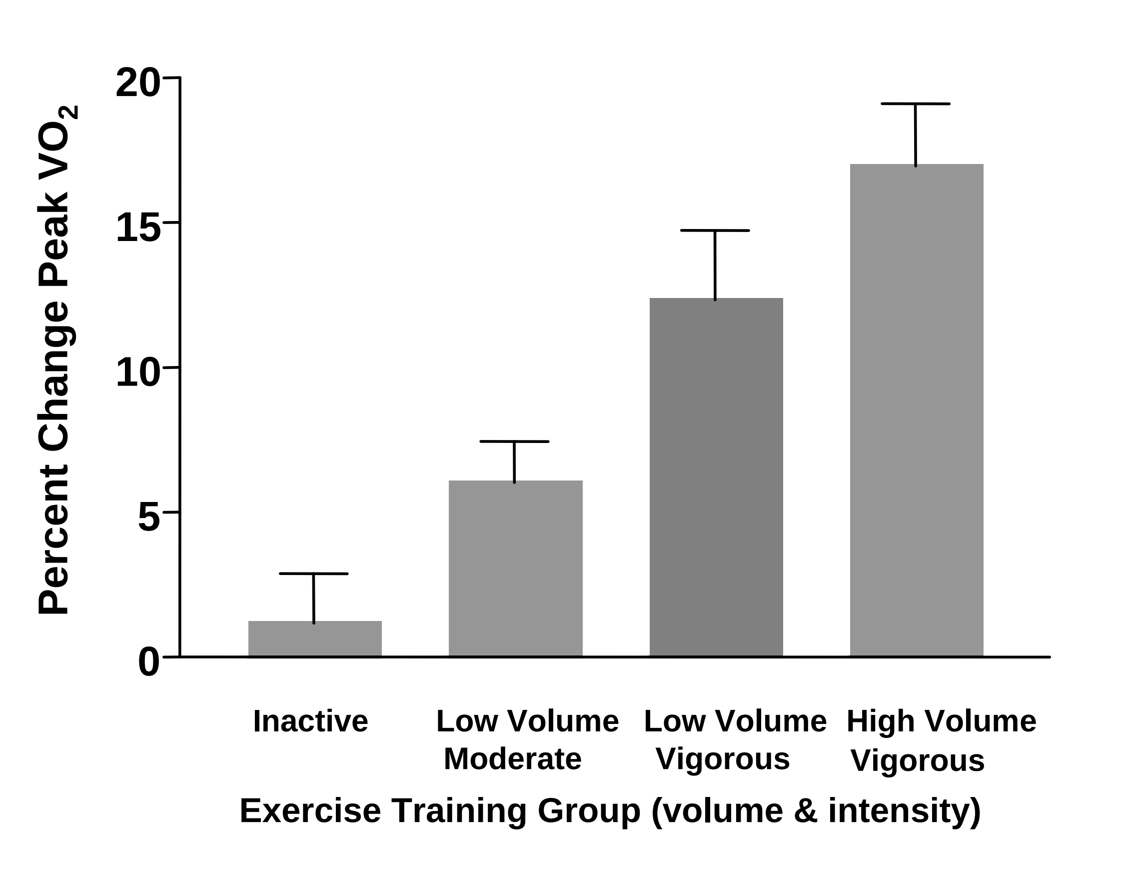

Figure G2.4. Changes in Peak VO_2 by Exercise Group and Ordered by Change

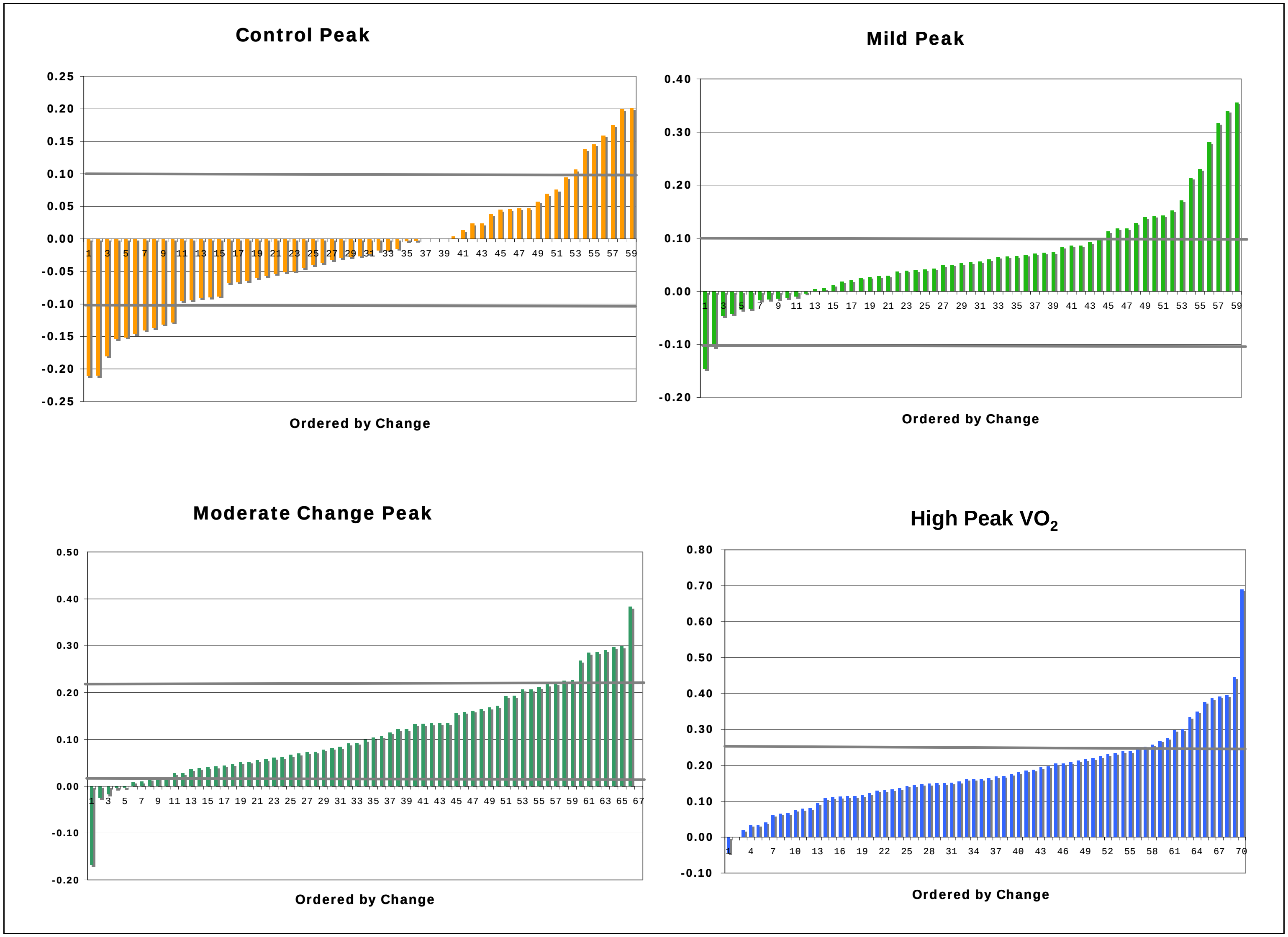

Figure G2.4. Data Points

Control Peak

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
26.88	21.22	0.79	-0.21
28.7	22.67	0.79	-0.21
24.55	20.13	0.82	-0.18
27.9	23.62	0.85	-0.15
23.8	20.2	0.85	-0.15
31.5	26.9	0.85	-0.15
29.55	25.4	0.86	-0.14
25.71	22.2	0.86	-0.14
35	30.4	0.87	-0.13
39.7	34.6	0.87	-0.13
29.4	26.6	0.90	-0.10
29.27	26.52	0.91	-0.09
25.3	23	0.91	-0.09
30.85	28.08	0.91	-0.09
20.4	18.6	0.91	-0.09
20.5	19.1	0.93	-0.07
42.4	39.6	0.93	-0.07
21.9	20.5	0.94	-0.06
32.39	30.44	0.94	-0.06
35.3	33.3	0.94	-0.06
28.1	26.6	0.95	-0.05
29.3	27.8	0.95	-0.05
37.77	35.9	0.95	-0.05
25.1	23.97	0.95	-0.05

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
27.6	26.5	0.96	-0.04
27.2	26.2	0.96	-0.04
21.4	20.7	0.97	-0.03
15.17	14.73	0.97	-0.03
36	35	0.97	-0.03
22.8	22.2	0.97	-0.03
30.69	30	0.98	-0.02
33.7	33.1	0.98	-0.02
28.5	28	0.98	-0.02
26.8	26.4	0.99	-0.01
33.5	33.4	1.00	0.00
34.9	34.8	1.00	0.00
21.6	21.6	1.00	0.00
26.5	26.5	1.00	0.00
27	27	1.00	0.00
26	26.1	1.00	0.00
37.3	37.8	1.01	0.01
21	21.5	1.02	0.02
29.4	30.1	1.02	0.02
18.7	19.4	1.04	0.04
17.9	18.7	1.04	0.04
34.98	36.57	1.05	0.05
21.3	22.3	1.05	0.05
21.3	22.3	1.05	0.05

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
24.4	25.8	1.06	0.06
23.1	24.7	1.07	0.07
30.4	32.7	1.08	0.08
17.57	19.23	1.09	0.09
25.3	28	1.11	0.11
21	23.9	1.14	0.14
24.1	27.6	1.15	0.15
25.8	29.9	1.16	0.16
19.81	23.27	1.17	0.17
18.1	21.7	1.20	0.20
22.4	26.9	1.20	0.20
27.9			
21.4			
33.8			
22.5			
22.7			
23.5			
28.6			
19.1			
33.6			
	32.75		
28.7			
33.43			
19.2			

Figure G2.4. Data Points (continued)

Mild Peak

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
23.9667	20.4667	0.85	-0.15
24.3333	21.7667	0.89	-0.11
30.6	29.2	0.95	-0.05
43	41.2	0.96	-0.04
20.5667	19.8667	0.97	-0.03
33.2966	32.1774	0.97	-0.03
29.6	29.1	0.98	-0.02
26.3	25.9	0.98	-0.02
22.1	21.8	0.99	-0.01
32.5	32.1	0.99	-0.01
21.3067	21.1	0.99	-0.01
26.4	26.3	1.00	0.00
23.8	23.9	1.00	0.00
18.1	18.2	1.01	0.01
24.8	25.1	1.01	0.01
27.6	28.1	1.02	0.02
24	24.5	1.02	0.02
42.5	43.6	1.03	0.03
22.2	22.8	1.03	0.03
31.3	32.2	1.03	0.03
24.815	25.5333	1.03	0.03
21.7	22.5	1.04	0.04
33.5	34.8	1.04	0.04
27.6	28.7	1.04	0.04
23.8833	24.8667	1.04	0.04
21.3	22.2	1.04	0.04
30.6	32.1	1.05	0.05
35.7	37.5	1.05	0.05
24.6	25.9	1.05	0.05

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
29.3	30.9	1.05	0.05
21.2	22.4	1.06	0.06
26.5	28.1	1.06	0.06
26.1	27.8	1.07	0.07
35	37.3	1.07	0.07
28.5	30.4	1.07	0.07
21.5907	23.0738	1.07	0.07
22.5	24.1	1.07	0.07
30.3	32.5	1.07	0.07
24.6	26.4	1.07	0.07
33.4	36.2	1.08	0.08
38.4	41.7	1.09	0.09
26.4373	28.7136	1.09	0.09
21.9033	23.9333	1.09	0.09
18	19.8	1.10	0.10
29.4755	32.803	1.11	0.11
31.4	35.1	1.12	0.12
19.5	21.8	1.12	0.12
24.1	27.2	1.13	0.13
17.84	20.3333	1.14	0.14
33.2833	38	1.14	0.14
26.5213	30.2995	1.14	0.14
20.1333	23.2	1.15	0.15
39.1	45.8	1.17	0.17
21.5	26.1	1.21	0.21
30	36.9	1.23	0.23
19.3667	24.8	1.28	0.28
24.6	32.4	1.32	0.32
22.023	29.503	1.34	0.34

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
22.8	30.9	1.36	0.36
17.7			
19.7			
24			
29.8			
21.3			
26.9			
22.3			
20.2			
24.3			
27.9			
26			
28			
20.8			
32.1			
27.3			
26.6			
26.3			
20.5			
22			
27.2			
22.4			
23.52			
17.94			
27.24			
27.89			
20.22			
33.6			
27.33			
22.35			

Figure G2.4. Data Points (continued)

Moderate Change Peak

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
28.3712	23.6123	0.83	-0.17
29.3333	28.6	0.98	-0.02
23.8	23.4	0.98	-0.02
26.8	26.7	1.00	0.00
35.7	35.6	1.00	0.00
21.5	21.7	1.01	0.01
26.7667	27.0333	1.01	0.01
37.2	37.8	1.02	0.02
36.3	36.9	1.02	0.02
39.3	40	1.02	0.02
39.7	40.8	1.03	0.03
32.4	33.3	1.03	0.03
35.1	36.4	1.04	0.04
20.7	21.5	1.04	0.04
25	26	1.04	0.04
33.188	34.5905	1.04	0.04
27	28.2	1.04	0.04
27.7	29	1.05	0.05
33.3	35	1.05	0.05
36.4	38.3	1.05	0.05
32.5	34.3	1.06	0.06
31.4333	33.2333	1.06	0.06
39.6	42	1.06	0.06
35.1	37.3	1.06	0.06
34.4	36.7	1.07	0.07
34.4	36.8	1.07	0.07
31.7	34	1.07	0.07
24.4	26.2	1.07	0.07
38.3	41.3	1.08	0.08
20.7	22.4	1.08	0.08

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
35.5	38.5	1.08	0.08
24	26.2	1.09	0.09
23.7	25.9	1.09	0.09
25.0233	27.5	1.10	0.10
26.1	28.8	1.10	0.10
25.4	28.1	1.11	0.11
33.1	36.9	1.11	0.11
31.2	35	1.12	0.12
28.6	32.1	1.12	0.12
30.2	34.2	1.13	0.13
34.0955	38.633	1.13	0.13
23.1	26.2	1.13	0.13
19.3	21.9	1.13	0.13
37.1	42.1	1.13	0.13
24.4	28.2	1.16	0.16
32.8	38	1.16	0.16
22.1533	25.7333	1.16	0.16
36.5	42.5	1.16	0.16
34	39.7	1.17	0.17
26.2	30.7	1.17	0.17
24	28.6	1.19	0.19
20.2	24.1	1.19	0.19
23.8	28.7	1.21	0.21
25.378	30.603	1.21	0.21
34.9	42.3	1.21	0.21
17.5	21.3	1.22	0.22
26.4	32.2	1.22	0.22
21.3	26.1	1.23	0.23
34.8	42.7	1.23	0.23
28	35.5	1.27	0.27

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
31.9	41	1.29	0.29
30.4	39.1	1.29	0.29
27.2	35.1	1.29	0.29
35.9016	46.5667	1.30	0.30
25.8	33.5	1.30	0.30
19.64	27.1667	1.38	0.38
17.8155	31.978	1.79	
21			
23.1			
22.8			
20.5			
19.3			
22.9			
31.3			
28.4			
23.9			
22.7			
17.3			
38.4			
37.5			
41.8			
37			
23			
26.1			
39.9			
33.1			
24.3			
22.3			
26			
21.9			

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
24.7			
35.4			
24.3			
32.9			
24.1			
25			
37.8			
37.4			
36.2			
27.2			
26.1			
26.6			
22.3			
20.7			
21			
27.4			
23.9			
21.8			
37.16			
26.8			
23.73			
22.9			
34.9			
15.8			
31.8			
26.04			
12.2			
17.81			
21.56			
18.01			

Figure G2.4. Data Points (continued)

High Peak VO_2

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
31.2714	29.8931	0.96	-0.04
24.2333	24.24	1.00	0.00
24.7	25.2	1.02	0.02
38.5	39.8	1.03	0.03
30.69	31.7367	1.03	0.03
29.6	30.8	1.04	0.04
36.9	39.2	1.06	0.06
35.3	37.6	1.07	0.07
31.6	33.7	1.07	0.07
34.1965	36.8	1.08	0.08
32.75	35.3333	1.08	0.08
26.1	28.2	1.08	0.08
31.7	34.7	1.09	0.09
20.2	22.4	1.11	0.11
25.0167	27.8	1.11	0.11
21.8615	24.3222	1.11	0.11
34.3	38.2	1.11	0.11
29.7643	33.1667	1.11	0.11
27.3	30.5	1.12	0.12
24.5333	27.5333	1.12	0.12
31.5	35.6	1.13	0.13
23.7	26.8	1.13	0.13
30.5	34.55	1.13	0.13
32.4667	36.9	1.14	0.14
27.3	31.2	1.14	0.14
28.3	32.4	1.14	0.14
36.1633	41.5333	1.15	0.15

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
25.5	29.3	1.15	0.15
22.4267	25.8	1.15	0.15
23.9	27.5	1.15	0.15
21.8	25.1	1.15	0.15
19.933	23.013	1.15	0.15
29.7	34.5	1.16	0.16
31.5	36.6	1.16	0.16
26.5	30.8	1.16	0.16
36.4	42.4	1.16	0.16
30.1	35.2	1.17	0.17
21.8	25.5	1.17	0.17
21.5	25.3	1.18	0.18
29.9	35.3	1.18	0.18
19.4	23	1.19	0.19
34.6	41.1	1.19	0.19
19.5	23.3	1.19	0.19
24.8	29.7	1.20	0.20
32.2	38.8	1.20	0.20
30.8533	37.2	1.21	0.21
20.2	24.4	1.21	0.21
25.3	30.7	1.21	0.21
24.13	29.35	1.22	0.22
32.3	39.4	1.22	0.22
32.3667	39.6333	1.22	0.22
35.9	44.2	1.23	0.23
33.3	41.1	1.23	0.23
30.6	37.9	1.24	0.24

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
21.3	26.4	1.24	0.24
31.4	39.2	1.25	0.25
20.2355	25.323	1.25	0.25
30.3	38.1	1.26	0.26
34.2	43.4	1.27	0.27
23.5	30	1.28	0.28
25.158	32.6655	1.30	0.30
33.3	43.3	1.30	0.30
26.3	35.1	1.33	0.33
29.5	39.8	1.35	0.35
29.9333	41.2	1.38	0.38
30.4357	42.2	1.39	0.39
33.2	46.2	1.39	0.39
22	30.7	1.40	0.40
28.1	40.6	1.44	0.44
17.1	28.9	1.69	0.69
14.5			
17.8			
27.2			
21.3			
18.3			
26.9			
25.6			
23.9			
26.3			
32.7			
27.8			

RVO_2_1	RVO_2_2	Diff 2-1	1-DX
35			
19.1			
26.5			
16.8			
30.6			
37.3			
18.8			
30.9			
30.5			
27.9			
27.3			
21.6			
20.9			
23.9			
23.7			
38.63			
25.33			
21.34			
27.12			
13.95			
23.39			
26			
27.16			
26.89			
18.79			
22.6667			

Table G2.2. Table of Baseline Characteristics, Exercise Prescriptions, Training Programs, and Outcome Measures in Two Randomized Controlled Aerobic Exercise Training Studies

Women: DREW (N~120) *

Group Prescriptions Training Volume (kcal/kg/wk)	Group Prescriptions Training Intensity (Percent Peak VO_2)	Baseline Peak VO_2 (mL/kg/min)	Training Program Training Prescription (MET-hr/wk)	Training Program Training Prescription (MET-min/wk)	Training Program Training METs	Training Program Training Minutes per Week	Change in Peak VO_2	Outcomes Change in Relative Peak VO_2 (mL/kg/min)	Outcomes Change in Peak VO_2 (METs)	Outcomes Change in Body Mass Index	Outcomes Change in Waist Circumference	Outcomes Change in Blood Pressure	Outcomes Change in Blood Lipids	Outcomes Change in FBG/ISI
4.0	50%	15.5	3.8	229	2.2	72	4.5%	0.70	0.20	NS	Decrease	NS	NS	NS
8.0	50%	14.9	7.6	457	2.2	136	7.0%	1.04	0.30	NS	Decrease	NS	NS	NS
12.0	50%	16.0	11.4	685	2.3	192	8.5%	1.36	0.39	NS	Decrease	Decr. SBP	NS	NS

Women: STRRIDE (N~30) †

Group Prescriptions Training Volume (kcal/kg/wk)	Group Prescriptions Training Intensity (Percent Peak VO_2)	Baseline Peak VO_2 (mL/kg/min)	Training Program Training Prescription (MET-hr/wk)	Training Program Training Prescription (MET-min/wk)	Training Program Training METs	Training Program Training Minutes per Week	Change in Peak VO_2	Outcomes Change in Relative Peak VO_2 (mL/kg/min)	Outcomes Change in Peak VO_2 (METs)	Outcomes Change in Body Mass Index	Outcomes Change in Waist Circumference	Outcomes Change in Blood Pressure	Outcomes Change in Blood Lipids	Outcomes Change in FBG/ISI
14.0	50%	23.4	13.3	800	3.3	193	6.5%	1.52	0.43	NS	NS	NS	Decr. TG	Lg. Incr. ISI
14.0	75%	23.9	13.3	800	5.1	134	14.3%	3.42	0.98	NS	NS	NS	NS	Incr. ISI
23.0	75%	24.1	21.9	1,314	5.2	195	16.4%	3.95	1.13	Decrease	Decrease	NS	NS	Incr. ISI

Men: STRRIDE (N~30) †

Group Prescriptions Training Volume (kcal/kg/wk)	Group Prescriptions Training Intensity (Percent Peak VO_2)	Baseline Peak VO_2 (mL/kg/min)	Training Program Training Prescription (MET-hr/wk)	Training Program Training Prescription (MET-min/wk)	Training Program Training METs	Training Program Training Minutes per Week	Change in Peak VO_2	Outcomes Change in Relative Peak VO_2 (mL/kg/min)	Outcomes Change in Peak VO_2 (METs)	Outcomes Change in Body Mass Index	Outcomes Change in Waist Circumference	Outcomes Change in Blood Pressure	Outcomes Change in Blood Lipids	Outcomes Change in FBG/ISI
14.0	50%	30.0	13.3	800	4.3	161	7.4%	2.22	0.63	Decrease	Decrease	NS	Decr. TG	Lg. Incr. ISI
14.0	75%	33.6	13.3	800	7.2	99	11.2%	3.76	1.08	NS	Decrease	NS	NS	Incr. ISI
23.0	75%	31.0	21.9	1,314	6.6	152	20.0%	6.20	1.77	Decrease	Decrease	Decr. SBP	Incr. HDL/ Decr. TG	Lg. Incr. ISI

Table G2.2. Table of Baseline Characteristics, Exercise Prescriptions, Training Programs, and Outcome Measures in Two Randomized Controlled Aerobic Exercise Training Studies (continued)

Men and Women: STRRIDE (N~60) †

Group Prescriptions Training Volume (kcal/kg/wk)	Group Prescriptions Training Intensity (Percent Peak VO_2)	Baseline Peak VO_2 (mL/kg/min)	Training Program Training Prescription (MET-hr/wk)	Training Program Training Prescription (MET-min/wk)	Training Program Training METs	Training Program Training Minutes per Week	Change in Peak VO_2	Outcomes Change in Relative Peak VO_2 (mL/kg/min)	Outcomes Change in Peak VO_2 (METs)	Outcomes Change in Body Mass Index	Outcomes Change in Waist Circumference	Outcomes Change in Blood Pressure	Outcomes Change in Blood Blood Lipids	Outcomes Change in FBG/ISI
14.0	50%	26.8	13.3	800	3.8	176	7.0%	1.88	0.54	NS	Decrease	NS	Decr. TG	Lg. Incr. ISI
14.0	75%	29.1	13.3	800	6.2	116	12.6%	3.67	1.05	NS	Decrease	NS	NS	Incr. ISI
23.0	75%	28.2	21.9	1,314	6	170	18.5%	5.22	1.49	Decrease	Decrease	NS	Incr. HDL/ Decr. TG	Lg. Incr. ISI

* Church, JAMA, 2007 (166)
† Duscha, Chest, 2005 (164); Johnson, Am J Cardiol, 2007 (158)
Decr., decreased; FBG, fasting blood glucose; HDL, high-density lipoprotein cholesterol; Incr., increase; ISI, insulin sensitivity index, a parameter of insulin sensitivity derived from a frequently sampled glucose tolerance test; lg., large; MET, metabolic equivalent; NS, not significant; SBP, systolic blood pressure; TG, triglycerides.

Similarly, changes in fitness in response to an exercise intervention can be expressed in percent change or absolute change. Examples of each of these in the two study populations are illustrated in this table. Because relative VO_2 is normalized to body mass, it is relatively sensitive to changes in body mass during interventions. The observation that relative fitness measures (relative peak VO_2) at baseline are 50% lower in DREW women than in STRRIDE women, may be due in part to the higher BMIs of DREW women (30-40 kg•m^{-2}) than in STRRIDE women (25-30 kg•m^{-2}) and demonstrates the sensitivity of maximal fitness measures, and exercise prescriptions when expressed as a percentage of baseline fitness to BMI. However, the difference in body mass between the women in these two study groups does not completely account for the differences in cardiorespiratory fitness, as the mean absolute peak VO_2 for women in DREW was approximately 1.2 L/min and 1.8 L/min in STRRIDE women. Similarly, women generally have lower cardiorespiratory fitness than do men and, therefore, the same relative intensity of exercise (e.g., 50% peak VO_2) represents a lower energy expenditure in women than it does in men. Relative percent increases in fitness in response to a fixed intervention is highly dependent on baseline fitness level, although absolute fitness measures are not. Finally, it is apparent that fitness changes do not correlate with all outcome measures in a monotonic and linear fashion (e.g., insulin sensitivity). Examination of these two studies in combination seem to indicate that at least 800 MET-minutes per week of physical activity are required to produce improvements in health outcomes, irrespective of the relative percent increases in cardiorespiratory fitness.

Effects of Daily Fractionization (Accumulation) of Exercise Bouts on Cardiorespiratory Fitness and Cardiovascular Health

Many groups are highly interested in whether multiple short bouts of exercise (e.g., 3 bouts of 10 minutes) is equivalent to one long bout (e.g., 1 bout of 30 minutes) per day for improving fitness levels. It should be evident that the choice of interval over which one integrates and accumulates a physical activity exposure (e.g., day, week, month, or year) is somewhat artificial, but interest remains in the issue of whether the benefits of activity are the same when total daily activity is divided over the course of the day. Several investigators have compared short versus long exercise regimens in an attempt to address this question (167-179). Data for this section were obtained from a literature search. From the appendix table (Table G2-A9, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/), it is apparent that these studies do not provide a clear answer to effects on cardiorespiratory fitness. Among these 11 studies, a single long bout of exercise was superior to multiple daily bouts in 3 studies of improving cardiorespiratory fitness. Multiple, shorter bouts were more effective in 2 studies, no difference was observed in 5 studies, and 1 study reported no improvement in either single long or multiple short exercise bouts. A pattern does appear to form within the few well-designed studies, however. It appears that both single long bouts and multiple shorter bouts of aerobic exercise training do elicit significant improvements in fitness, and that the evidence is relatively strong that comparable fitness responses can be achieved with different fractionization of the volume, given that the daily volume of the exposure is the same.

Several factors likely play a role in the variability of the findings. Careful analysis of demographics and methods of each study indicate that the populations under study differ widely, from college students to middle aged and overweight individuals. It is possible that the more sedentary an individual is at baseline (e.g., the lower the peak VO_2), the less a difference is observed in fitness responses when the exposure is fractionated over the course of the day. This may be due to the fact that less fit individuals are exercising at lower absolute intensities (e.g., walking) and that fractionation has less influence on fitness responses when the intensity of the exercise is lower. If true, then as fitness levels increase, fitness responses should be more dependent on how the exposure is fractionated. This concept has not been tested but begs for further work.

Second, these studies differed quite a bit in exercise exposures (e.g., intensity, frequency). The intervention length ranges from 8 weeks to 18 weeks, while the intensity varies from 50% to 60% of predicted heart rate maximum to 70% to 80% of heart rate reserve. This variation is reflected in the large range of fitness changes reports, from no change to as much as 19% improvement. For example, in a study of young college students who trained at 50% to 60% of predicted heart rate maximum, no improvement in cardiorespiratory fitness was reported. It is very possible that the exercise exposure was not adequate for this population. That is, it is possible that one cannot distinguish the differences in responses between long and short bout activities when the total volume of the stimulus is insufficient to generate optimal responses—for example, where the total exercise time is fixed at 30 minutes of moderate-intensity activity, and a longer period of moderate-intensity activity or the same period of vigorous-intensity activity might better distinguish the responses to bout duration when total exercise volume is held constant. Moreover, although these studies report their results as fitness gains, not all studies use the same fitness measures. Many of the studies do not perform a maximal exercise test and only extrapolate a maximal value based upon a sub-maximal test.

Third, the other outcomes in these studies, cardiovascular risk markers, such as lipids, glucose control, and others show various responses to the interventions. When responses differ, the continuous exposure regimens seem to have more favorable outcomes than do fractionated regimens, although the data are too limited to provide a reliable estimate of the effects of fractionated exercise on such outcomes.

Overall Summary and Conclusions

The weight of evidence points toward a favorable relation between increases in habitual dynamic aerobic exercise and cardiovascular health outcomes, including coronary heart disease morbidity and mortality, stroke, control of blood pressure, atherogenic dyslipidemia, vascular function measures, and cardiorespiratory fitness. In addition, dynamic aerobic exercise is considered a standard of therapy for increasing functional performance in peripheral arterial disease. In many of these outcomes, including cardiovascular morbidity and mortality, there appears to be a more favorable response with increasing intensity of exercise bouts, although exercise volume is poorly controlled in some studies and may be the important mediating exercise parameter. Also, the more powerful relation between exercise intensity and outcomes does not hold for all outcomes in experimental studies, especially when weekly volume or energy expenditure is held constant (160). In many, if not most, cardiovascular outcomes, favorable responses are notable and reproducible when the volume of physical activity exceeds 800 MET-minutes per week. A combination of endurance exercise bouts with different intensities, durations, and frequencies per day and week can achieve this level of exercise, which is approximately equivalent to 12 miles per week of walking or jogging at any intensity. As energy expenditure at a given perceived intensity is highly dependent upon baseline fitness level, sex, and type of activity, a volume target can be individualized with adjustment of bout intensity, duration, and frequency, both initially and as greater fitness levels are achieved. Given that more volume is likely to result in greater benefits but also higher injury and cardiovascular risk, the ultimate volume goal should be approached gradually upon the initiation of a program, especially in initially sedentary individuals.

Research Needs

In the course of reviewing the literature that contributed to the information presented in this chapter, several significant deficiencies in the published literature became apparent. More information addressing the following issues would have significantly improved the information base used to formulate physical activity recommendations. The Cardiorespiratory Health subcommittee encourages governmental agencies to highlight research in these areas before the next iteration of the *Physical Activity Guidelines for Americans.*

1. What is the time course of acquisition of the cardiovascular health benefits resulting from increases in habitual physical activity?

2. What are the cardiovascular health benefits of varying exercise bout duration, frequency, and intensity, while controlling for total volume?

3. What effect does daily exercise exposures accumulated in short bouts have on the acquired cardiovascular health benefits of habitual physical activity?

4. What are the effects of resistance training on cardiovascular health and what is the nature of dose-response effects (varying intensity, bout volume, and frequency of programs)?

5. Are there sex differences in cardiovascular health benefits of habitual exercise when controlling for volume?

6. What are the specific harmful effects of physical inactivity on cardiovascular health?

7. Are there responses that differ by ethnic and racial minority differences?

8. What are the specific effects of aerobic training, resistance training, and a combination on selected biomarkers of vascular health, such as brachial artery flow-mediated dilation? What are the dose-response effects?

9. What are the main characteristics of an exercise program for preventing and treating peripheral artery disease? What are the exercise dose-response patterns, sex differences, exercise modality options, and differential effects on diabetic patients with PAD, on asymptomatic patients, and are there biomarkers to predict exercise responders?

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Part G. Section 3: Metabolic Health

Introduction

Metabolic syndrome and diabetes are highly significant public health problems in the United States. Ford and colleagues (1) estimate, based on government surveys, that 47 million people in the United States have metabolic syndrome. It is also estimated that 20.8 million Americans (about 7% of the US population) have type 1 diabetes (T1D) or type 2 diabetes (T2D), of whom only two thirds have been diagnosed and the remaining one third are unaware of their condition (2;3). The great majority (estimated to be 90% or more) of these individuals have T2D. The prevalence of diabetes is higher among persons of Hispanic, African American, and Native American background than among persons of non-Hispanic white origins. The majority of deaths in persons with diabetes are caused by cardiovascular disease (CVD), including myocardial infarction and stroke. People with diabetes not only have a high prevalence of manifestations of atherosclerosis but also have increased prevalence of cardiovascular (CV) risk factors, including hypertension and the dyslipidemias. Alarmingly, type 2 diabetes, once called adult-onset diabetes because it chiefly presented in middle-aged persons, is now appearing in ever younger people, and its prevalence in adolescents and children is increasing rapidly. The potential ramifications of T2D in adolescents and children has yet to be determined.

Exercise and physical activity play a clear role in preventing and treating metabolic syndrome and T2D as well as the macrovascular complications of T2D. The importance of the role of exercise and physical activity is highly important and is of increasing interest both in the United States and in other countries as well, as the magnitude of the public health problems of metabolic syndrome and diabetes continues to increase and as solutions are being sought. The role of physical activity and exercise in treating T1D is less well established than for T2D, although evidence suggests that benefits are likely, perhaps most of all in the area of reducing mortality, CVD risk factors, and microvascular complications. For both T1D and T2D, physical activity may prevent the development of diabetic neuropathy and diabetic nephropathy. Finally, it appears likely that physical activity and exercise may help prevent and treat gestational diabetes although more research is needed to further establish these findings.

Review of the Science

Overview of Questions Asked

This chapter considers 6 major questions dealing with the potential role of physical activity and exercise in preventing and treating metabolic syndrome, T1D and T2D, common complications of diabetes, and gestational diabetes:

1. Does physical activity have a role in preventing or treating metabolic syndrome?
2. Does physical activity have a role in preventing and treating type 2 diabetes?
3. Does physical activity have a role in reducing macrovascular risks in type 2 diabetes?
4. Does physical activity have benefits for type 1 diabetes?
5. Does physical activity have a role in preventing and treating diabetic microvascular complications?
6. Does physical activity and exercise have a role in preventing and treating gestational diabetes?

Data Sources and Process Used To Answer Questions

The Metabolic Health subcommittee used the *Physical Activity Guidelines for Americans* Scientific Database as its primary source of references for the topics covered in this section of the report (see ***Part F: Scientific Literature Search Methodology,*** for a full description of the Database). The Database contains studies published in 1995 and later. In its search, the subcommittee used broad study selection criteria, which included: all age groups; all study designs; all physical activity types as well as cardiorespiratory fitness; disease conditions including T2D, T1D, diabetic nephropathy/neuropathy/retinopathy, metabolic syndrome, gestational diabetes, hypoglycemia, glucose, and insulin.

Studies were also identified through computerized searches of several databases, including PubMed, CINAHL, Health Plan, Cochrane Collaboration, and Best Evidence. Standard MESH terms often were only partially successful in identifying relevant articles. Articles also were found through a combination of searching published reference lists as well as references from meta-analyses and systematic reviews.

Question 1. Does Physical Activity Have a Role in Preventing or Treating Metabolic Syndrome?

Conclusions

Regular physical activity is associated with reduced risk of metabolic syndrome (Tables G3.A1, G3.A2, G3.A3, and G3.A4, which summarize these studies, can be accessed at http://www.health.gov/paguidelines/report/.). The available data demonstrate an inverse dose-response association between level of activity and risk of metabolic syndrome, with the minimal amount of activity to prevent metabolic syndrome ranging from 120 to 180 minutes per week of moderate-intensity physical activity, and many studies supporting a goal of 150 minutes per week. The findings derived from studies using self-report measures of physical activity are similar to those studies in which cardiorespiratory fitness was measured. The dose-response association between physical activity and prevention of metabolic syndrome is similar in men and women. Although limited data support the use of exercise for the treatment of metabolic syndrome, this is an area in great need of more work, as is the role of physical activity in preventing and treating metabolic syndrome in youth (Table G3.A5, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.) and across ethnicities.

Introduction

A number of clinical criteria, such as those of the National Cholesterol Education Program and World Health Organization (4), have been developed to define the metabolic syndrome. These criteria are very similar and share the following cluster of characteristics: abnormal levels of lipids (low high-density lipoprotein and high triglycerides), elevated glucose, hypertension, and excess abdominal obesity (5-8). This review is not limited to any specific clinical definition of metabolic syndrome but rather includes any report in which the definition of metabolic syndrome was consistent with the above characteristics.

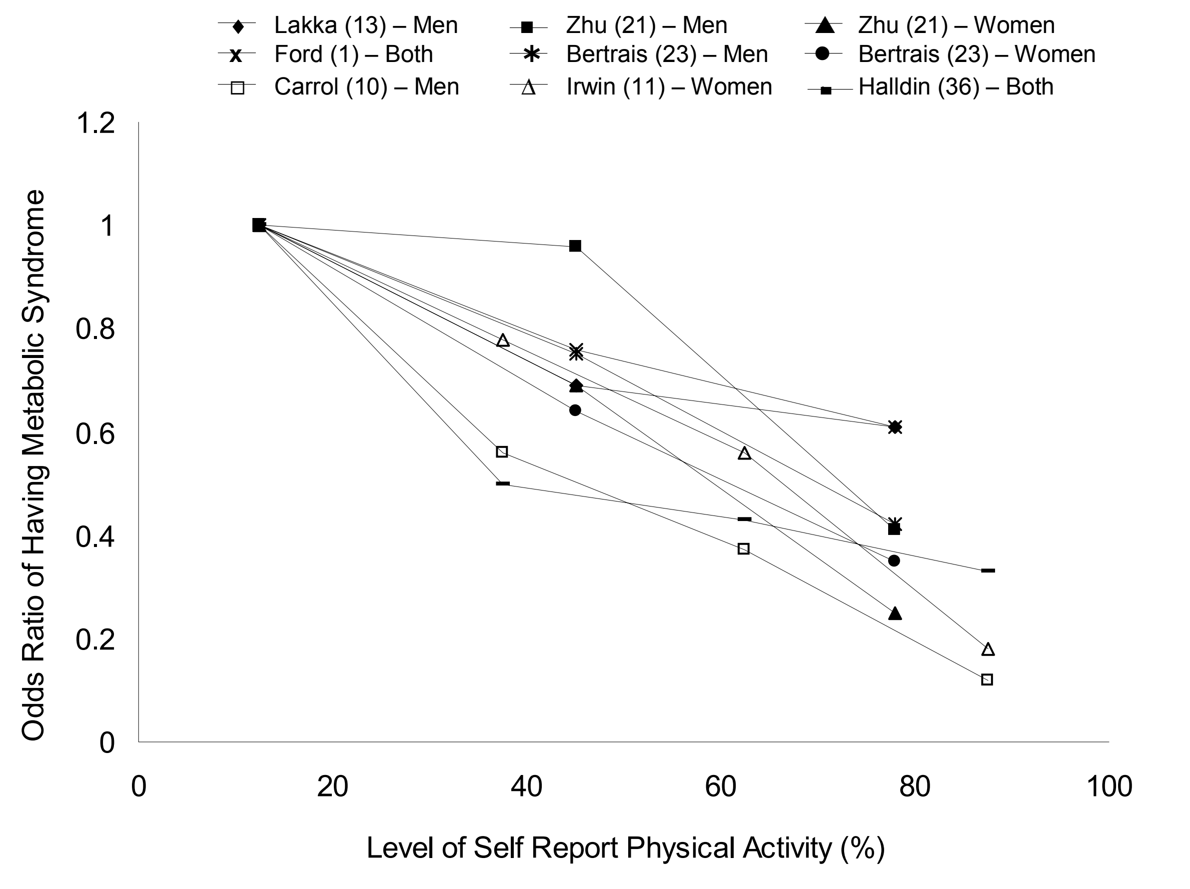
Rationale

In general both cross-sectional and longitudinal cohort studies consistently show a lower incidence and prevalence, respectively, of metabolic syndrome among physically active individuals as compared with their inactive peers (9-45).

Dose-Response Relation

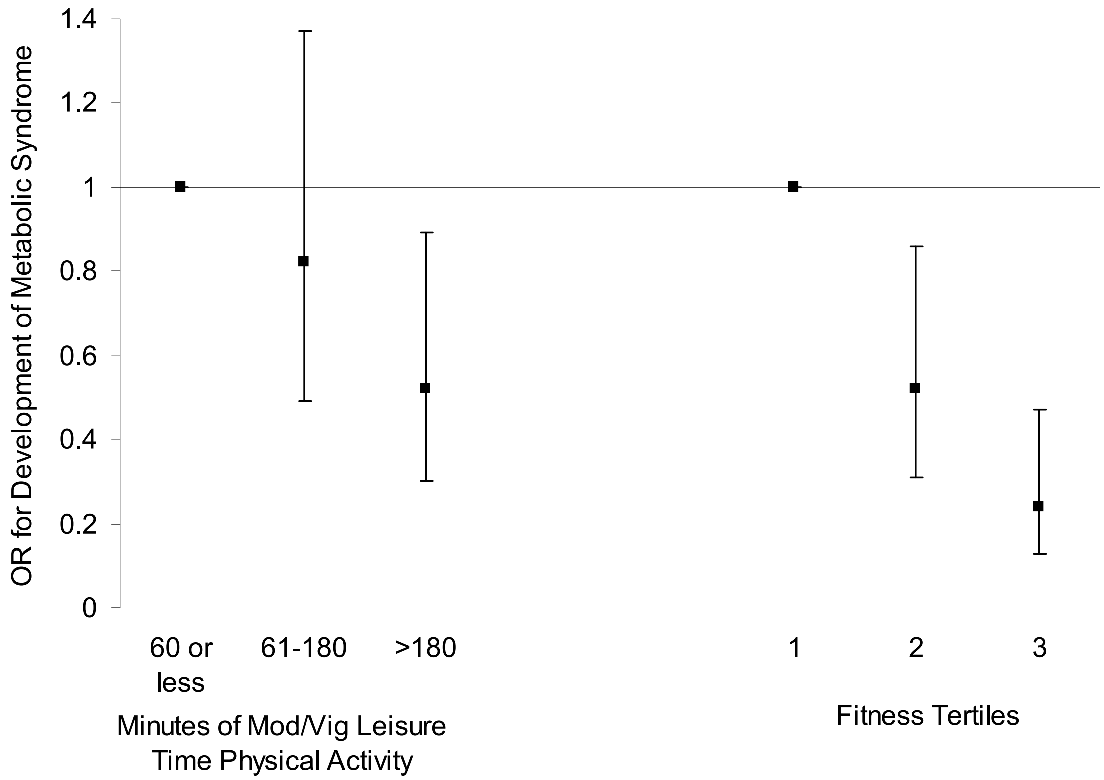
In the cross-sectional studies, which examined the prevalence of metabolic syndrome across levels of physical activity and primarily used questionnaires to obtain self-report data (Figure G3.1), (Table G3.A.3, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.), all found an inverse gradient between amount of physical activity and metabolic syndrome (10;11;13;21;23;26;36).

Figure G3.1. Summary of Cross-Sectional Physical Activity and Metabolic Syndrome Studies Using Categories of Physical Activity That Could Be Used To Examine Dose-Response



From the cross-sectional studies in which minutes per week of moderate-intensity physical activity for each category were provided or could be estimated, 120, 150, and 180 minutes or more per week of moderate intensity activity have all been reported as minimum amounts associated with reduced prevalence of metabolic syndrome (13;23;26;36). It should be noted that these studies used different methods of activity assessment, the activity categories have large ranges, and the cut-points for the activity categories were not similar or generated using the same statistical methods. None of the studies was designed or powered to analyze the minimal dose of activity to prevent metabolic syndrome. However, the cross-sectional data supports that obtaining at least 120 to 180 minutes per week of moderate-intensity physical activity is consistently associated with a lower prevalence of metabolic syndrome. Only the 2002 report from Laaksonen and colleagues (Figure G3.2) provides data that could be used to examine the dose-response between physical activity and the development of metabolic syndrome (41).

Figure G3.2. Data Prospectively Demonstrating That Both Higher Levels of Physical Activity and Fitness Protect Against the Future Development of Metabolic Syndrome



Source: Laaksonen et al. (41)

Figure G3.2. Data Points

Development of Metabolic Syndrome	Time Physical Activity Low	Time Physical Activity Middle	Time Physical Activity High	Fitness Tertiles Low	Fitness Tertiles Middle	Fitness Tertiles High
Odds Ratio	1	0.66	0.55	1	0.59	0.36

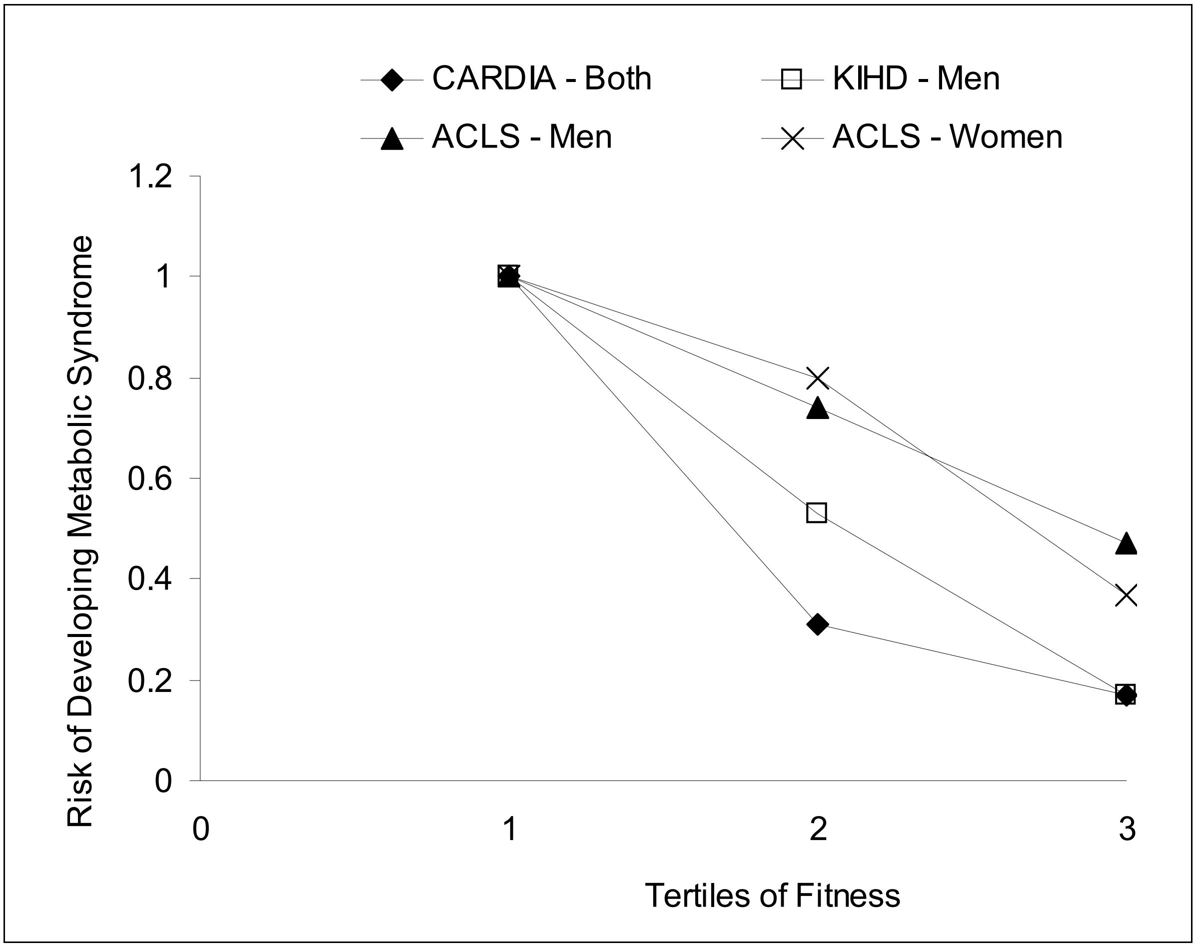
The results were similar to those from the cross-sectional studies. A dose-response relation exists between level of activity and risk of developing metabolic syndrome, with 180 or more minutes per week of moderate intensity physical activity being the minimal amount of time associated with reduced risk of developing metabolic syndrome.

Physical Activity Level Versus Cardiorespiratory Fitness

Laaksonen and colleagues also measured cardiorespiratory fitness and, as depicted in Figure G3.2 and Table G3.A1, the inverse dose-response relationship associated with prevention of metabolic syndrome, is even stronger than that seen with questionnaire-assessed self-report of physical activity (41).

All available prospective studies that measured fitness and categorized participants based on fitness level similarly show a strong inverse dose-response between fitness and risk of developing metabolic syndrome (Figure G3.3) (39;41;46-48) .

Figure G3.3. Summary of Longitudinal Fitness and Metabolic Syndrome Studies That Used Categories of Fitness To Examine Dose-Response Relations



CARDIA, Coronary Artery Risk Development in Young Adults; KIHD, Kuopio Ischemic Heart Disease Risk Factor Study; ACLS, Aerobic Center Longitudinal Study

Thus, despite the methodological differences in assessing physical activity through self-report (questionnaire) vs. measured cardiorespiratory fitness, the association with the prevention of metabolic syndrome is similar for these two modes of activity assessment.

Sex Differences

The available data are composed of men-only studies, women-only studies, and combined-sex studies, with no one type of study comprising the preponderance of the data. As demonstrated in Figure G3.1, the physical activity-metabolic syndrome association is similar in men and women, indicating that both men and women benefit from participating in regular physical activity. As demonstrated in Figure G3.3, the fitness-metabolic syndrome association also is similar in men and women. Thus, no matter whether studies using self-reports of physical activity or objective measures of fitness, it appears that no sex differences exist in regard to the benefits of physical activity in preventing metabolic syndrome.

Youth

Only very limited data are available for youth. These studies, using a variety of methods to quantify physical activity and define metabolic syndrome, are consistent with the findings in adults, namely that higher levels of activity and fitness are associated with reduced risk of metabolic syndrome (Table G3.A5, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.) (15;44;49;50;50-53). However, this topic is deserving of future study and investigation.

Effect of Race and Ethnicity

The majority of studies with large sample sizes were conducted in Europe or were composed of persons of American or European descent. Though some of the better studies were conducted in populations composed of both African Americans and whites, no studies have examined the physical activity-metabolic syndrome association in an African American or Mexican American population only (11;26;46). Thus, the data on the relationship between physical activity or fitness in terms of preventing metabolic syndrome in non-white populations are limited, and this is clearly an area that needs additional research. It should be noted that in the studies that used study populations composed of both non-Hispanic whites and African Americans, such as the National Health and Nutrition Examination Survey (NHANES) and the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a strong dose-response relation between activity (or fitness) and prevention of metabolic syndrome was evident (26;46).

Prolonged Sitting and Other Sedentary Behaviors

Although regularly participating in physical activity and not leading a sedentary lifestyle may appear to be synonymous, evidence suggests that these two behaviors should be treated as different dimensions of the same pubic health issue. In other words, it is important not only to obtain adequate amounts of aerobic exercise but also to avoid extreme sedentary behaviors, such as prolonged sitting. This is obviously of great importance in today's environment, in which the typical work day is characterized by long bouts of sitting and most non-work hours are spent watching television. Available data suggest a direct relationship between the prevalence of metabolic syndrome and the time spent watching television or using the computer (23;25;26). For example, using NHANES data (n=1,626 men and women), Ford and colleagues observed that individuals who reported watching television or using the computer 4 or more hours a day had a 2 times greater risk of having metabolic syndrome compared to individuals who reported less than 1 hour a day of television or computer use (26). Given that the current environment in the United States promotes sedentary behavior both within and outside the work place, strategies for reducing sedentary behavior, in addition to promoting exercise, have great potential public health impact.

Role of Physical Activity in Treating Metabolic Syndrome

Numerous studies have examined the benefits of exercise training on individual components of metabolic syndrome, such as blood pressure or fasting glucose. In general, improvements to the variables of interest are noted with exercise training. However, no published studies have been specifically designed to examine the efficacy of exercise training in the reversal of the clinical diagnosis of metabolic syndrome. Two reports have conducted post-hoc analyses to examine the role of exercise in reversing metabolic syndrome. Using data from the HERITAGE study, Katzmarzyk and colleagues report that 20 weeks of aerobic training were associated with improvements in triglycerides, blood pressure, fasting glucose, and waist circumference among 105 participants who had metabolic syndrome at baseline (54). Further, the prevalence of metabolic syndrome decreased 30.5% in this sub-set of participants who received exercise training. However, this study was not controlled, which makes the interpretation of this data challenging. In a recent manuscript using data from the dose-response STTRIDE study, Johnson and colleagues observed an improvement in waist circumference, triglycerides, and blood pressure when the included exercise groups (walking or jogging exercise in varying intensities) (n=130) were combined. None of these variables changed in the control group (n=41) (55). The prevalence of metabolic syndrome also decreased in the combined exercise group from 41% to 27%, with no change in prevalence of metabolic syndrome in the control group (39% to 46%). Although these preliminary data generated from post hoc analyses suggest that exercise training may be an important therapeutic option for the treatment of metabolic syndrome, this area needs additional research. In particular, clinical exercise trials prospectively designed and powered to examine the efficacy of exercise in treating metabolic syndrome are needed.

Resistance Training

Very few studies have examined the role of resistance training or quantified muscular strength in preventing or treating metabolic syndrome (56-58). In both a cross-sectional and longitudinal report from the Aerobic Center Longitudinal Database, greater muscular strength was associated with lower risk of metabolic syndrome (56;57). However, in the report using longitudinal data, the degree of risk reduction associated with greater levels of strength was attenuated (from −34% to −24%) when cardiorespiratory fitness was adjusted for (57). Given the important role of skeletal muscle in insulin sensitivity, developing a better understanding of the role of resistance training in the prevention and treatment of metabolic syndrome is an area of great interest.

Question 2. Does Physical Activity Have a Role in Preventing and Treating Type 2 Diabetes?

Conclusions

Increased levels of physical activity are associated with significantly decreased risks of developing T2D. Most of the studies addressing T2D prevention have focused on vigorous activity, but a number have included walking at moderate intensity, which has proven efficacious as well. Importantly, two randomized controlled trials (RCTs) and results of observational studies provide empiric evidence to support 150 minutes per week of moderate intensity physical activity for T2D prevention. Several studies have shown that 30 minutes per day of moderate intensity exercise 5 days per week are effective in preventing T2D. Available data do not enable minimal recommendations, although some of the large observational studies show that any amount of increased physical activity is associated with T2D prevention. Recommendations are valid for both men and women. Data are insufficient to clearly show that the benefits are uniform across all ethnicities and racial groups but no data support a lack of benefit and available data do support the benefit in these groups.

Introduction

As noted at the beginning of this chapter, diabetes is a highly significant public health problem in the United States. Available data reveal that physical activity has a strong role in the prevention and treatment of T2D. These data include results from observational studies, and RCTs as well as physiological studies related to physical activity and/or exercise. The relationship between T2D and cardiovascular fitness also is important because population studies reveal a direct correlation between all-cause mortality and reduced fitness in persons with T2D (59;60). Following are data that support the importance of physical activity and exercise in the prevention and treatment of T2D as well as a discussion of the safety of exercise for persons with T2D.

Rationale

Observational Studies of Physical Activity in Preventing Type 2 Diabetes

Large prospective cohort and cross-sectional observational studies that assessed physical activity through the use of questionnaires all show that increased physical activity levels are associated with reduced risk for developing T2D. As with the assessments looking at the relationship between metabolic syndrome and physical activity, it should be noted that these studies used different methods of activity assessment, the activity categories have large ranges, and the cut-points for the activity categories were not generated using the same statistical methods. In addition, none of the studies was designed or powered to analyze the minimal dose of activity to prevent T2D. Importantly though, however the studies were conducted, the benefit of physical activity in preventing T2D is consistently present. Major prospective cohort studies are described here to illustrate the range of methods used and results obtained. Meta-analyses and structured reviews on this topic are summarized in Table G3.A6, which summarizes these studies and can be accessed at http://www.health.gov/paguidelines/report/. These studies reveal that both moderate and vigorous physical activity can prevent T2D. Dose-response summary information is provided separately below.

In a study by Helmrich and colleagues (61) in 5,990 male alumni of the University of Pennsylvania, incidence rates of T2D decreased as energy expenditure in leisure time physical activity in kilocalories per week increased from less than 500 to 3,500. They found that for each 500 kilocalorie increment in leisure-time physical activity, the age-adjusted risk of T2D was reduced by 6% (relative risk [RR]=0.94, 95% CI= 0.90-0.98) (61). In a study by Manson and colleagues (62) in the Nurses' Health Study cohort (87,252 US women aged 34 to 59 years), the investigators found that women who engaged in vigorous exercise at least once per week had an age-adjusted RR of 0.67 when compared to women who did not exercise (*P* <0.0001). This significant benefit persisted even after adjustment for body mass index (BMI) although results were somewhat attenuated by this measure (62). Hu and colleagues (63) compared the benefits of walking with benefits of vigorous physical activity on risk of developing T2D in the Nurses' Health Study. Physical activity was divided into quintiles in this study. The authors found that walking (considered a moderate intensity form of exercise) as well as vigorous activity were associated with decreased risk of T2D, with greater physical activity levels providing the most benefit. A study of 5,159 British men revealed a decreased risk for developing T2D that progressively decreased with increasing levels of physical activity (64). Participants were sorted into one of 6 defined levels of physical activity ranging from inactive to vigorously active based on frequency and intensity of the physical activities of each participant. The authors found that the age-adjusted relative risk of T2D decreased progressively with increasing levels of physical activity with even moderate physical activity having a significant effect. In a study of 6,013 Japanese men, Okada and colleagues (65) found that those who engaged in regular physical exercise at least once a week had a relative risk of T2D of 0.75 (95% CI, 0.61-0.93) compared with men not engaging in exercise. In a cohort of 34,257 women aged 55 to 69 years, Folsom and colleagues determined that any level of physical activity was associated with a decreased risk of developing T2D (RR=0.69, 95% CI=0.63, 0.77) when compared with sedentary behavior (66). In a study assessing the effects onT2D of physical activity in 37,918 healthy men where activity levels were classified in metabolic equivalent (MET)-hours per week and considered either moderate or vigorous, relative risks for T2D across increasing quintiles of MET-hours per week were 1.00, 0.78, 0.65, 0.58, and 0.51 (*P* for trend <.001) (67). Walking pace also was assessed in this study, and walking was found to be efficacious for preventing T2D. Hu and colleagues (68) assessed data from 6,898 Finnish men and 7,392 women ranging in age from 35 to 64 years to evaluate the relationship of occupational, commuting, and leisure-time physical activity with the incidence of T2D.

After adjustment for potential confounders, the hazards ratios of diabetes associated with light, moderate, and active work were 1.00, 0.70, and 0.74 respectively (P=0.020 for trend) and the authors concluded that high or moderate levels of activity were associated with a reduced risk of T2D (68). In a prospective cohort study of 37,878 women, a participant was considered active if she expended more than 1,000 kilocalories on recreational activities per week, with activity levels being divided into quartiles (69). Physical activity was an independent predictor of T2D in this study although BMI was a more powerful predictor. In the Women's Health Initiative Observational Study, Hsia and colleagues (70) found that physical activity across exercise quintiles was associated with a decreased risk of T2D particularly in non-Hispanic white women. This was true for walking (multivariate-adjusted hazard ratios 1.00, 0.85, 0.87, 0.75, 0.74; P for trend <0.001 across exercise quintiles) and total physical activity score (hazard ratios 1.00, 0.88, 0.74, 0.80, 0.67; P=0.002).

These data demonstrate a strong inverse relationship of physical activity across quintiles with diabetes risk in non-Hispanic white women and men. Associations in women of other races and ethnicites are less clear, but the authors of one study (70) note that the study may not have been adequately powered to fully assess data from particular race or ethnic subgroups or possibly that physical activity levels among these groups may not have been intense enough to allow for analyses (see section below).

Physical Activity Level Versus Cardiorespiratory Fitness

Similar to the questionnaire studies, observational studies that assessed physical activity levels using objective measures of cardiorespiratory fitness reported that better fitness is associated with a reduced risk of developing T2D (71-73). Lynch and colleagues (71) found that in a population-based sample of 897 middle-aged Finnish men, higher cardiorespiratory fitness was associated with lower risk of developing T2D compared to sedentary persons. Wei and colleagues (60;72) found that low cardiorespiratory fitness (measured during a maximal exercise test) and physical inactivity (measured by self-report) were associated with risk of impaired fasting glucose and T2D as well as all-cause mortality in men with T2D. In the former study, after adjusting for potential confounders, men in the low-fitness group (the least fit 20% of the cohort) at baseline had a 1.9-fold risk (95% CI, 1.5- to 2.4-fold) of impaired fasting glucose and a 3.7-fold risk (CI, 2.4- to 5.8-fold) of T2D compared with those in the high-fitness group. In another study, in which cardiorespiratory fitness was measured during an exercise test and the 6,249 female participants were divided into thirds by level of fitness, Sui and colleagues (73) found that compared with the least fit third, the adjusted hazard ratio was 0.86 (95% CI=0.59-1.25) for the middle third and 0.61 (95% CI=0.38-0.96) for the upper third of cardiorespiratory fitness. Similar to results from studies using self-report data, results from these studies overall suggest a benefit for achieving and maintaining increased levels of physical activity (64;66;74;75).

Randomized Controlled Trials of Type 2 Diabetes Prevention

The difficulty of evaluating many of the large RCTs looking at the effects of physical activity or exercise on diabetes prevention has been to sort out the effects of diet versus physical activity, as these treatments are commonly combined in large trials. Three large

RCTs have assessed the role of physical activity independently, either using trial design or by analytic means (Table G3.A7, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.). The Da Qing Impaired Glucose Tolerance and Diabetes Study in China (76) included an exercise-only treatment arm and found that even modest changes in exercise, without change in diet, reduced the risk of developing diabetes. The exercise prescription in this study was 1 or 2 units of exercise a day, with units defined in terms of intensity and duration. One unit was equal to 20 minutes of "mild" exercise (e.g., slow walking, shopping, housekeeping), 20 minutes of "moderate" exercise (e.g., fast walking, cycling), or 10 minutes of "strenuous" exercise (e.g., slow running, stair climbing) or 5 minutes of very strenuous exercise (e.g., skipping, basketball). In this trial, which was randomized by clinic rather than by participant, diabetes risk was reduced 46% in the exercise group, 42% in the diet and exercise group, and 31% in the diet-treated group.

The Diabetes Prevention Study in Finland (77;78) and the Diabetes Prevention Program in the United States (79) have provided clear evidence that intensive lifestyle modifications, including strong diet and physical activity interventions, reduce the risk of developing T2D. Importantly, the role of physical activity is independently beneficial to preventing diabetes. In the Diabetes Prevention Study, 522 middle-aged, overweight men and women with impaired glucose tolerance (IGT) were randomized to either lifestyle modification or a control group (77;78). The physical activity prescription portion of the lifestyle modification (which included a strong dietary component) was for 30 minutes a day of moderate exercise for a total of more than 4 hours per week. Incidence of diabetes was very significantly reduced in the intervention group.

In the Diabetes Prevention Program, 3,234 men and women with IGT and impaired fasting glucose were randomized into control, medication (i.e., metformin, a drug commonly used to treat T2D), or lifestyle modification groups. The physical activity prescription portion of the lifestyle arm (which also had a strong dietary component) was 150 minutes of activity per week. The lifestyle component reduced incident diabetes by 58% and had a more powerful effect than metformin (by 39%). In the Diabetes Prevention Program and Diabetes Prevention Study, weight loss was the dominant predictor of a reduced incidence of diabetes. However, recent analyses from these studies showed that increased levels of physical activity prevented diabetes even after adjusting for confounders (80-82).

Physiological Data Showing Benefits of Exercise in Treating Type 2 Diabetes and Elucidating the Role of Cardiorespiratory Fitness

Type 2 Diabetes is associated with reduced exercise capacity (83;84). Maximal oxygen consumption was approximately 20% lower compared to nondiabetic persons of similar weight and physical activity levels in these studies. These exercise abnormalities are present even in the absence of diabetes-related complications and even in persons with recently diagnosed T2D. The abnormalities are likely associated with cardiac and hemodynamic abnormalities (85-87).

It has been well established that a single bout of moderate exercise has a profound effect on glucose metabolism that may last up to about 18 hours (88). In addition, repeated bouts of exercise appear to have a cumulative beneficial effect on glucose metabolism. A meta-analysis (89) including 14 studies, provides evidence that regular moderate-intensity exercise improves metabolic control in T2D. This meta-analysis shows that exercise significantly improves glycemic control and reduces visceral adipose tissue and plasma triglycerides, although not plasma cholesterol, in people with T2D, even in the absence of weight loss. Exercise training in persons with T2D also has a very significant effect in terms of improving maximal oxygen consumption, measures of submaximal exercise performance, and other measures of fitness (e.g., 90;91). Available data suggest that these findings are true for African American women (92) as well as white women. These findings are further discussed in the section on preventing macrovascular complications of T2D.

Dose-Response Relation

Data on exactly how much physical activity is needed in order to prevent T2D are limited because such studies have not been prospectively designed. Data from observational studies indicate that the amounts of effective physical activity range from any increase over sedentary levels to moderate and vigorous activity levels. It appears, therefore, that any physical activity may be better than none in terms of preventing diabetes, but better results are achieved if individuals engage in higher intensity and more frequent physical activity. Data from several studies support that approximately 30 minutes of moderate intensity exercise at least 5 days per week provides a substantial (25% to 36%) reduction in the risk of T2D according to the Nurses' Health Study (63), the Iowa Women's Health Study (66), the Study of Eastern Finns (68), and the Diabetes Prevention Program (79). Importantly, several of the prospective cohort studies discussed above included walking as a specific modality of physical activity and all of these found that walking was beneficial in terms of preventing T2D compared to sedentary behavior (61;63;67;69;70). Thus, data from observational studies and RCTs support the current recommendation that 2.5 hours per week or typically 30 minutes a day for 5 days a week be performed to prevent T2D. Jeon and colleagues (75) performed a meta-analysis on the prospective cohort studies that assessed the preventive effects of moderate-intensity physical activity that could be analyzed independent of vigorous-intensity physical activity. Moderate-intensity physical activity was defined as an activity requiring 3.0 to 6.0 METs (75). They identified 10 cohort studies that met these criteria. These studies in total included 301,121 participants and 9,367 incident cases. Five of the studies specifically included walking. The summary RR of T2D was 0.69 (95% CI 0.58-0.83) among participants who regularly participated in moderate-intensity exercise compared to sedentary counterparts. The RR for T2D was 0.70 (0.58-0.84) for walking on a regular basis (typically briskly for 2.5 hours per week or more) compared to no walking. However, no data are available to support a specific recommendation for a minimal or even a lesser dose of exercise. In addition, it is not clear how much additional risk reduction is obtained with higher levels of physical activity.

Sex and Race/Ethnicity Differences

In observational studies that included women only, 3 large US cohort studies (67-70) all found that greater physical activity was associated with a lower incidence of diabetes. However, in one study, this relationship was present only in non-Hispanic white women and not in women of African American, Hispanic or Asian descent (70). These findings await confirmation in further studies because the study may not have been powered to detect differences across all race or ethnic groups. Results were based on self report of diabetes in the total population but were confirmed in a subset who also provided blood samples and physician reports.

Data from RCTs as well as observational studies suggest clearly that overall, increased levels of physical activity play a beneficial role in preventing T2D for both women and men. In the Diabetes Prevention Program (93), treatment effects did not differ significantly according to sex, race, or ethnic group. Lifestyle factors addressed in the Program included diet and physical activity, and both had an independent effect on preventing T2D. Although participant numbers became too small for clear results when grouped by ethnicity, it appears that risk reduction compared with placebo was greater for the lifestyle group than for the metformin group in non-Hispanic whites (50% versus 12%, respectively) and Hispanics (57% versus 2%, respectively) (94). African Americans (42% versus 29%) and Native Americans (43% versus 42%), showed similar efficacy for the lifestyle and metformin groups. However, for Asian Americans, metformin showed a nonsignificantly greater reduction than intensive lifestyle intervention (62% versus 30%). Neither lifestyle nor metformin showed significant heterogeneity across the 5 ethnic groups in terms of efficacy. Subsequent studies in India and Japan (95;96), as well as the Da Qing study in Chinese people (76), similarly found an independent effect of physical activity in preventing T2D, and the findings were true for men and women and appeared to be true for all ethnic groups involved.

Thus, overall, acknowledging the limited data available to date, no strong evidence is available to negate the data suggesting that physical activity prevents T2D in men and women of different race and ethnic groups, although further research should explore this important issue.

Youth

Type 2 Diabetes is growing in prevalence in children and adolescents. Alarmingly, unlike youth who do not have T2D, youth with this condition often have CV risk factors, such as hypertension and dyslipidemias as well. Thus, potentially, youth who have T2D may develop CVD at relatively young ages (97;98). Data from RCTs show that increased physical activity improves insulin sensitivity in obese youth, although longitudinal data are limited (99-101) and the effects on CV risk factors are not well established because trials are lacking. A recent review has highlighted the efforts of different interventions to address obesity in youth of various ethnic and racial groups. These interventions focused on lifestyle changes including increased physical activity (102), and several had a physical activity-only component (103;104). Overall findings were encouraging. The studies of both Sallis and colleagues (103) and Pangrazi and colleagues (104) showed that school-based programs promoting increased physical activity were effective at increasing the physical activity level or cardiorespiratory endurance (although not in reducing BMI) of girls especially.

No RCTs have been completed that show that physical activity or exercise prevents T2D in youth although it is likely give results in aduls. To date, the limited intervention and observation studies suggest that to prevent and manage T2D, daily goals for youth should include less than 60 minutes of daily screen (television, computer or video game) time and 60 to 90 minutes of daily physical activity (105-107). A large multicenter trial (the TODAY study) is currently underway to assess the role of physical activity in preventing T2D in youth (108).

Resistance Training

Resistance training has shown promise as a modality for **treating** diabetes (109;110). Sigal and colleagues (111) found, in a group of 251 individuals with T2D, that both aerobic and resistance training individually improved glycemic control, but improvements were greatest with combined aerobic and resistance training. However, this exercise modality has not been explored for its role in prevention of T2D in large trials, and no data currently exist showing that resistance training plays a role in preventing T2D. Future studies should further investigate the role of resistance training in preventing T2D given the beneficial effects of such training on the metabolism of persons with T2D.

Safety of Physical Activity and Exercise for Persons With Type 2 Diabetes

The consensus is that the benefits of exercise for persons with T2D far outweigh the risks. However, safety concerns about exercise in this group have been voiced. These concerns range from cardiovascular risks associated with physical activity and exercise to caution about hypoglycemia and foot care concerns. The American Diabetes Association (ADA) guidelines on safety (112;113) provide a comprehensive review of safety issues and measures, although the recommendations lack supporting data in some cases.

Question 3. Does Physical Activity Have a Role in Reducing Macrovascular Risks in Type 2 Diabetes?

Conclusions

Strong data support the benefits of physical activity and fitness for CVD protection in T2D and IGT. The data are stronger for hard outcomes, such as CVD events and mortality, than for known CVD risk factors, but this may be an artifact of the relatively short duration of risk factor studies and the potential for small changes in risk factors to have a large cumulative impact on outcomes. These data suggest that a minimum of moderate-intensity aerobic activity for more than 2 hours per week is necessary to achieve significant benefit, and that near maximum benefit may be achieved with moderately vigorous aerobic activity, such as brisk to very brisk walking, for 3 to 7 hours per week (about 12 to 21 MET-hours per week). Combined aerobic and resistance activity appears to have greater benefits than either type alone when CVD risk factors (and non-CV effects) are considered, but CVD outcome data for activity other than aerobic activity are lacking. In general, the existing data for CVD risk reduction in persons with T2D are consistent with a recommendation of an aerobic activity program with a goal of at least 120 minutes per week and preferably more than 180 minutes per week of moderate to moderately vigorous activity.

Rationale

Several studies have specifically considered the effects of physical activity on CVD risk factors and outcomes in T2D. Observational studies have shown that, among persons with this condition, those who exercise or are more fit have a reduced risk of CV morbidity and mortality than do less active or less fit individuals (67;114-118) (Tables G3.A8 and G3.A9, which summarize these studies, can be accessed at http://www.health.gov/paguidelines/report/.). A study of more than 3,000 Finns with T2D found that all types of physical activity (e.g., recreational and occupational) are beneficial in reducing CV events and mortality (117). Following is a review of the evidence for benefits, dosage, and type of physical activity specifically for reduction of CVD risk and outcomes in T2D.

Cardiovascular Disease Risk Factor Reduction

Many cross-sectional studies have found inverse correlations between physical activity level and various CVD risk factors in T2D populations. Two meta-analyses of these studies have been performed (119;120). One focused on lipid effects and hemoglobin A1c (HbA1c) and found a small (5%) but significant decrease in low-density lipoprotein (LDL) cholesterol (−6.4 mg/dl, range = −11.8 to −1.1) and a strong trend toward improved HbA1c (−0.4%, range = −0.8 to 0.0), but no change in total cholesterol or triglycerides (120). This section focuses on a recent meta-analysis of controlled intervention studies in subjects with T2D that compared different exercise interventions for their effects on CVD risk factors (119). The meta-analysis covers about 1,000 subjects, aged 48-62 years. Exercise interventions were of aerobic, resistance, or combined types. Overall conclusions from the analysis were that all forms of exercise improved insulin sensitivity, with combined types having the greatest effect (especially in men) and resistance alone the least. Combined exercise also had small and moderate benefits on systolic and diastolic blood pressure, respectively, and a small benefit on raising high-density lipoprotein (HDL) levels. Aerobic exercise also benefited triglyceride levels and systolic blood pressure. Resistance exercise did not show significant benefit on any CVD risk factor. Another recent prospective trial with a 6-month, twice weekly, progressive, supervised aerobic program in a population with T2D also demonstrated improved HDL levels (12%) and marked decreases in markers of endothelial dysfunction (ICAM-1 and P-selectin), but no changes in inflammatory markers (hsCRP and TNF-alpha) or LDL levels (121).

Cardiovascular Disease Outcomes

Only one intervention study and no randomized trials have addressed the effect of activity or fitness on hard CVD outcomes. The ongoing Look AHEAD (Action for HEAlth in Diabetes) trial, currently underway, is a randomized long-term study addressing hard CV outcomes after an intervention (122-124). However, the intervention is targeted at weight loss by a combined program of diet and physical activity and thus will not address the effect of physical activity in isolation. In the one existing interventional trial looking at physical activity alone, Shinji and colleagues followed a small group (n=102) of T2D adults for 17 months after institution of a single, modest, home-based exercise program (walking 20 to 30 minutes, 4 to 6 times per week, at anaerobic threshold) (125). Incident CVD was much higher in "dropouts" than in "completers" even after adjustment for multiple parameters with a RR for incident CVD of 16.5 (95%CI, 1.19-228) for dropouts versus completers. This study suggests that low-level physical activity is beneficial for primary CVD prevention in people with T2D. However, no data were reported or adjustments made for smoking or diet, the "dropouts versus completers" study comparison was nonrandomized, the number of events was very small (n=8), and the confidence interval was very large.

Several prospective cohort studies have found that CV fitness (60;126-128) (Table G3.A8) and physical activity level (60;67;115-118;129;130) (Table G3.A9) are inversely correlated with mortality (all-cause and CVD) and/or CVD event rates in subjects with T2D. Some of these studies have evaluated the effect of frequency, duration, and/or intensity of physical activity on the protective effect. A follow-up of the National Health Interview Survey of 2,896 adults with T2D (115) found that walking for more than 2 hours per week (but not more than 0 hours to 1.9 hours) was associated with a significantly decreased hazard ratio (HR) for CVD mortality (HR = 0.59, 95% CI 0.40 to 0.87, *P* for trend 0.03 after exclusion of disabled subjects, and after adjusting for age, sex, race, BMI, self-rated health, smoking, weight loss approaches, hospitalizations, hypertension or medications, physician visits, limitations caused by CVD or cancer, and extent of functional limitation).

In the Nurses' Health Study of more than 5,000 diabetic women followed for 14 years, subjects were placed in 5 groups based on hours of total moderate-vigorous activity per week, including non-leisure activities (67). RR for CVD events (fatal and nonfatal myocardial infarction or stroke) decreased progressively with increasing weekly volume of moderate to vigorous activity (less than 1, 1 to 1.9, 2 to 3.9, 4 to 6.9, and 7 or more hours per week). Age-adjusted relative risks were 1.0, 0.93 (95% CI, 0.69 to 1.26), 0.82 (95% CI, 0.61 to 1.10), 0.54 (95% CI, 0.39 to 0.76), and 0.52 (95% CI, 0.25 to 1.09) (*P* for trend <0.001). This relationship did not change appreciably after adjustment for smoking, BMI, and other CV risk factors. Among women who primarily walked for exercise, both increased pace (easy pace: 1.0, average pace: 0.52, brisk pace: 0.47, *P* for trend 0.001) and weekly MET walking score were inversely associated with CVD event risk. Among women who did not exercise vigorously in addition to walking, multivariate relative risks across quartiles of MET scores for walking were 1.0, 0.85 (0.62-1.34), 0.63 (0.36-1.10), 0.56 (0.31-1.00) (*P* for trend 0.03) for 0 to 0.5, 0.6 to 2.7, 2.8 to 7.5, and more than 7.5 MET hours per week of walking.

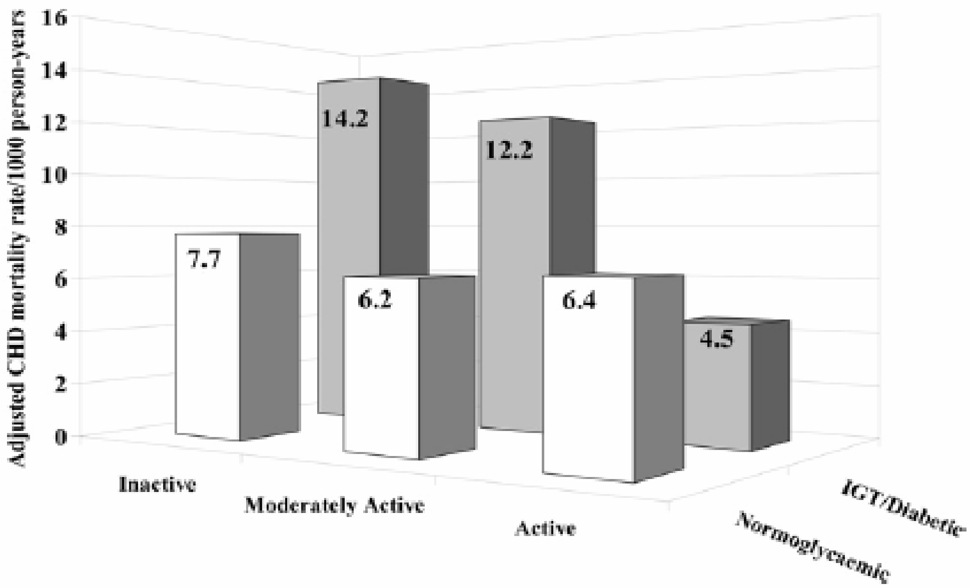
In the Health Professionals follow-up study, Tanasescu and colleagues followed about 2,800 men with T2D for 14 years and assessed incident CVD (fatal or nonfatal MI or stroke) (116). Risk of total and fatal CVD events showed a statistically significant improvement with increasing physical activity after age-adjustment (*P* for trend 0.02, 0.03, respectively) and a strong trend after multivariate analysis (adjusted for alcohol intake; smoking; family history of myocardial infarction; use of vitamin E supplements; duration of T2D; diabetes medication; quintiles of dietary intake of trans fat, saturated fat, fiber, and folate; history of angina and coronary artery bypass graft; and baseline presence of hypertension and high serum cholesterol; *P* for trend 0.07, 0.13, respectively). Additional adjustment for BMI further attenuated the trend (for total CVD events: 1.0, 0.91 [0.63-1.31], 0.68 [0.45-1.02], 0.76 [0.51-1.14], and 0.72 [0.47-1.09] by quintile; *P* for trend 0.14). Their results suggest that physical activity protects from CVD events, especially fatal events, and that for T2D, moderate energy expenditure (3rd quintile, 12 to 22 MET-hours per week, corresponding to about 3 to 5 hours per week of brisk walking) provides the most protection. The authors state that this was not the case in the non-diabetic cohort where a more continuous dose-response was seen. A separate walking intensity multivariate analysis suggests that for those who walked for exercise, the higher the walking speed, the greater the protection. After adjustment for CVD risk factors, walking time, and other vigorous activity, the relative risks for normal pace (2 to 2.9 miles per hour), brisk pace (3 to 3.9 miles per hour), and very brisk pace (more than 4 miles per hour) were 0.82, 0.58, and 0.17 (95% CI 0.04 to 0.71; *P* for trend <0.001) compared to an easy pace (less than 2 miles per hour).

The studies described above suggest that maximum benefit may be achieved with substantial volumes of moderately vigorous exercise, such as brisk to very brisk walking, for 3 to 7 hours per week. It is interesting to speculate that subjects with T2D may differ from non-diabetic subjects in their response to very vigorous exercise, but further studies are needed to fully address the intensity response of CVD risk reduction with physical activity in T2D.

In the Whitehall Study, Batty and colleagues performed a comparative study of the benefits of physical activity in men with T2D or IGT (Table G3.A9) compared to men with normal glucose tolerance (131). After adjustment for other factors, physical activity remained an independent predictor of all-cause, CHD, and other CVD mortality. The gradient for benefit with increasing physical activity was much steeper for the IGT/T2D subjects than for those with normal glucose tolerance, suggesting a greater benefit for metabolically impaired subjects than for the general population. A plot adapted from this data illustrates that the highest level of physical activity actually eliminated the excess CHD mortality associated with IGT and T2D (132) (Figure G3.4).

Others have also found a steeper response of CVD risk to physical activity in diabetic subjects, but most studies have found that CVD risk remains greater in diabetic than non-diabetic subjects even in the most active subgroups (116).

Figure G3.4. Physical Activity/Exercise and Macrovascular Risk Reduction in Type 2 Diabetes



Note: Age-adjusted cardiovascular disease mortality rates by leisure time activity in normoglycemic men (n=6,056) versus men with impaired glucose tolerance/diabetes (n=352) in the Whitehall Study (Adapted by Gill and Malakova 2006, (132) from data from the Whitehall Study). *P*=0.006 for trend in normoglycemic men, *P*=0.003 for trend in men with IGT/diabetes.

Source: Gill JM, Malkova D. Physical activity, fitness and cardiovascular disease risk in adults: interactions with insulin resistance and obesity. Clin Sci (Lond). 2006 Apr;110(4):409-425. Review. Reproduced with permission.

Physical Activity, Cardiovascular Fitness, and Type 2 Diabetes

A recent meta-analysis evaluated the benefits of physical activity for CV fitness in persons with T2D (133). The overall analysis of 9 randomized, controlled, prospective interventional studies had mean exercise characteristics of 3.4 sessions per week and 49 minutes per session for 20 weeks. Mean baseline maximal oxygen consumption of 22.4 ml/kg/min increased 11.8% in the exercise arms and decreased 1.0% in the control arms. Magnitude of improvement in maximal oxygen consumption and in HbA1c correlated better with exercise intensity than with exercise volume. Because fitness and glycemic control appear to benefit overall and CVD mortality, this suggests that more intense exercise would have greater mortality benefits. However, the possibility of a mortality impact of intense exercise in diabetic people cannot be ruled out and is, in fact, suggested by some outcome studies (discussed above). Furthermore, overt nephropathy, peripheral neuropathy, and retinopathy present in many diabetic individuals may be contraindications to very vigorous activity, prolonged stepping activities, and weight-lifting or high-impact activities, respectively, though these recommendations appear to be based on little experimental evidence (see Question 5. Does Physical Activity Have a Role in Preventing and Treating Diabetic Microvascular Complications?).

Question 4. Does Physical Activity Have Benefits for Type 1 Diabetes?

Conclusions

Data are more limited for type 1 diabetes (T1D) than for T2D, but generally support benefits of exercise for T1D in reducing mortality, CVD risk factors, and microvascular complications. Data are weaker for benefits for glycemic control, and CVD outcomes have not been studied. Data regarding the optimal exercise prescription also are limited. This may still include limiting exercise appropriately in proliferative retinopathy. However, any exercise prescription in T1D also must address the issue of avoiding exercise-induced hypoglycemia. This requires an individualized approach that includes modifying insulin dosing, ingesting additional carbohydrates, and ensuring appropriate details of the exercise prescription.

Rationale

Though T1D is less prevalent than T2D, it remains among the most prevalent chronic, serious diseases of childhood affecting about 1.5/1,000 children in the United States (134). Overall prevalence estimates are increasing now that it has been recognized that a quarter to a half of all T1D develops in adults. Although the metabolic abnormalities associated with insulin resistance have not been considered major factors in this autoimmune form of diabetes, CVD has long been known to be a major cause of morbidity and mortality in T1D. It is now becoming recognized that insulin resistance is also present in T1D and that this may contribute to the associated excess CVD risk. As T1D individuals spend a longer portion of their lives with absolute endogenous insulin deficiency and relative insulin sensitivity, hypoglycemia is a greater safety concern in T1D than in T2D. Effects of physical activity on CVD risk factors and glycemic control and safety concerns are addressed in this section. Microvascular complication effects are addressed in a later section (see Question 5. Does Physical Activity Have a Role in Preventing and Treating Diabetic Microvascular Complications?).

As with T2D and non-diabetic populations, exercise has been shown to be inversely correlated with mortality in T1D. In a cohort study of 548 T1D subjects followed for 7 years in the Pittsburgh Insulin-dependent Diabetes Morbidity and Mortality Study, sedentary males were 3 times as likely to die as active males (135). The relationship did not achieve statistical significance in women.

Physical Activity and Type 1 Diabetes Prevention

No data exist to show that habitual physical activity or exercise plays a role in preventing T1D.

Physical Activity and Type 1 Diabetes Treatment

Glycemic Control

Exercise increases insulin sensitivity and induces non-insulin dependent skeletal muscle glucose uptake. Overweight or otherwise insulin resistant T1D individuals will derive benefit from the improvement in insulin sensitivity that accompanies exercise in the same way that T2D individuals do (see Question 1. Does Physical Activity Have a role in Preventing or Treating Metabolic Syndrome?). Recent evidence suggests that even apparently insulin sensitive diabetic individuals are insulin resistant compared to non-diabetic controls (136;137). Theoretically, therefore, most or all T1D patients might be expected to improve insulin sensitivity with physical activity. As such, it would seem that exercise could improve glycemic control. However, for a T1D patient on a regular dose of insulin, this improved sensitivity comes at the cost of an increased risk of hypoglycemia and resultant hyperglycemia. Furthermore, high-intensity exercise increases catecholamine release and can cause post-exercise hyperglycemia. Thus, studies have had mixed results. Nevertheless, the largest studies have demonstrated improved glycemic control with physical activity in T1D. Interventional studies, most from the 1980s, have all been small (Table G3.A10, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.). Most have used a moderate aerobic exercise program and have had mixed results, with some negative (138-144) and some modestly positive (145-148) trials. One of the positive trials included a "carbohydrate control" diet intervention in addition to exercise (145). Thus, the improved glycemic control in this study cannot clearly be attributed to exercise. Other positive studies did not include any dietary change or monitoring. Some negative trials followed caloric intake and noted an increase in calories in the exercise group (139). Few studies have looked at resistance training. Two studies with resistance interventions were split, one with improvement in HbA1c (148), the other without (143). Larger cross-sectional studies have also been split (Table G3.A11, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.). Ligtenberg studied 200 subjects and found no correlation between self-reported activity and HbA1c (149). The FinnDiane study of 1,030 T1D subjects found a sex-based difference in that self-reported physical activity did correlate with improved HbA1c in women, but not in men (150). The effect on HbA1c in women was an 0.5% decrease in both the moderately active (10 to 40 MET-hours per week) and active groups (more than 40 MET-hours per week). In contrast, in men, insulin doses were decreased to a greater extent in the more active populations. In the largest study to date, Herbst and colleagues studied more than 23,000 subjects with T1D and found a small, but highly significant improvement in HbA1c (0.3%) in the 2 active groups (exercise 1 to 2 times a week and 3 or more times a week) compared to the sedentary group (151). Only one study compared resistance to aerobic training and found no benefit for glycemic control in either arm (143). Overall, good evidence for a significant role for exercise alone in glycemic control is limited. Existing evidence suggests that a modest improvement in glycemic control occurs with small amounts of activity and does not increase with more frequent or more intense exercise. More studies are needed to further clarify the role of physical activity in T1D because many of the studies are relatively old.

Macrovascular Complications

CVD risk factors. The FinnDiane study found that low physical activity correlated with the presence of metabolic syndrome in TID, especially the waist circumference component (152). Lehman and colleagues found significant improvements in insulin sensitivity, LDL, HDL, blood pressure, and waist-to-hip ratio with a self-monitored increase in physical activity of about 150 minutes per week without an increase in severe hypoglycemic events (153). Few studies have investigated the effect of different doses or types of exercise on CVD risk factors in TID. In one 12-week intervention study, Ramalho and colleagues compared the effects of thrice weekly 40 minutes of moderate aerobic training to resistance training (143). Neither group improved lipid profiles, but the aerobic group had improved waist circumference while the resistance group did not.

CVD outcomes. No data exist on the effect of physical activity on actual CV outcomes specifically in T1D.

Physical Activity, Type 1 Diabetes, and Risk of Hypoglycemia

Whatever the benefits of exercise in T1D, it is clear that they come at the expense of an increased risk of hypoglycemia, both during and up to 30 hours after exercise. However, the ADA Position Statement on Physical Activity and Exercise states the “all levels of physical activity, including leisure activities, recreational sports, and competitive professional performance, can be performed by people with T1D who do not have complications and are in good glucose control”(154, p.61). This is because it is possible, with a good understanding of the physiologic responses to exercise, to manage exercise and post-exercise blood sugars. Guidelines for hypoglycemia control have been published, although they are not always strongly data-based and therefore are outside the scope of this section. (155-162).

Question 5. Does Physical Activity Have a Role in Preventing and Treating Diabetic Microvascular Complications?

Conclusions

Physical activity may prevent the development of diabetic neuropathy and diabetic nephropathy (primary prevention) in those with T1D and T2D. Though uncontrolled observational studies suggest physical activity may treat diabetic neuropathy and nephropathy, RCTs are necessary to confirm this. Other observational studies suggest no effect of physical activity on either the prevention or treatment of diabetic retinopathy in T1D subjects. No data are available on sex differences or dose-response of physical activity.

Moderate-intensity physical activity appears safe for all individuals with diabetes even those with existing diabetic microvascular complications, although vigorous-intensity activity, high-impact exercise, or weight-bearing exercise may possibly lead to adverse outcomes in those with existing proliferative retinopathy, severe nephropathy with renal osteodystrophy, or severe neuropathy, respectively. Exercise stress testing is not recommended before starting a moderate-intensity exercise regimen and is of controversial benefit before initiating a vigorous intensity aerobic exercise program.

Introduction

Persons with diabetes have a highly increased prevalence of microvascular complications, which are associated with substantial morbidity. In this section, the role of physical activity in preventing and treating microvascular complications in those with T1D and T2D will be discussed. For the purpose of this document, microvascular complications of diabetes are defined to include neuropathy (based either on symptoms, physical examination, or abnormal electromyogram findings consistent with this diagnosis), nephropathy (defined as microalbuminuria, macroalbuminuria, or decreased calculated glomerular filtration rate), and retinopathy (defined as non-proliferative or proliferative retinopathy diagnosed by an ophthalmologist using retinal photographs).

To date, no large RCTs have investigated the role of exercise training or physical activity in preventing or treating diabetic microvascular complications. One small RCT and some observational studies have suggested a possible relationship between physical activity and both the primary prevention and treatment (tertiary prevention) of diabetic microvascular complications. One meta-analysis (119) has evaluated the impact of physical activity on a surrogate intermediate marker (HbA1c) for progression to diabetic microvascular complications, and showed convincingly that physical activity interventions lower HbA1c. Because better glycemic control has been shown to decrease the incidence of diabetic microvascular complications in subjects with T1D (163) and T2D (164), it is possible that exercise training could reduce microvascular complications solely due to its general improvement of glycemic control. However, the overall lack of studies in this area means that the role of physical activity in preventing microvascular complications remains inconclusive. Specific gaps in the literature that warrant further research are large studies to determine the exercise dose-response curve for prevention or treatment of microvascular complications, and determining whether differences exist by subject race/ethnicity, sex, T1D vs. T2D, or exercise modality.

The next three sections will summarize what is known regarding the role of physical activity in preventing and treating 1) diabetic neuropathy, 2) diabetic nephropathy, and 3) diabetic retinopathy. Safety concerns for exercise in these populations also will be discussed.

Rationale

Observational studies provide most of the existing data, which are of limited scope and quality, to determine the role of physical activity in primary prevention of diabetic nephropathy, neuropathy, and retinopathy. Observational studies of lesser quality (often uncontrolled) have been performed to address the role of physical activity for treatment of diabetic nephropathy, neuropathy, and retinopathy. To determine the safety of physical activity with existing microvascular complications, small observational studies have been performed and clinical standards of care also have been discussed when appropriate to supplement the scarce amount of safety data.

Diabetic Neuropathy

One small RCT (165), one cross-sectional study (166), and one retrospective cohort study (167) have evaluated the impact of physical activity on primary prevention of diabetic neuropathy (Table G3.A12, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.). From these limited data, no firm conclusions may be drawn but it does appear that physical activity may possibly have some role in preventing diabetic neuropathy. The RCT data, although only based on 78 participants (73% with T2D), revealed a reduction in both motor and sensory neuropathy from 4 years of moderate-intensity exercise despite no significant weight loss (165). Of the 2 cross-sectional studies performed in T1D subjects addressing neuropathy, one showed physical activity significantly benefited males only (166), while the other had no effect (167).

Treatment of Diabetic Neuropathy

No studies have evaluated the use of physical activity to treat diabetic neuropathy. One study evaluated 12 months of physical activity in conjunction with a dietary intervention for prediabetic neuropathy (Table G3.A13, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.), using a pre-post study design in 40 subjects with prediabetes to show significant differences in nerve fiber density at the proximal portion of the leg ($P < 0.05$), and non-significant improvement in neuropathic pain and nerve fiber density at the distal portion of the leg (168).

With respect to diabetic ulcer prevention in a group with diabetic neuropathy, no significant improvement in the surrogate outcome of dorsal foot cutaneous perfusion was found after either a 10-week aerobic exercise (169) or 8-week resistance exercise program (170). Although significant differences were initially described in dorsal foot cutaneous perfusion between physically active individuals with T2D as compared with sedentary individuals with T2D who had a higher mean HbA1c (171), no differences were evident when this study was repeated with similar HbA1c levels between groups (172). This area requires further study.

Safety of Exercise With Diabetic Neuropathy

Three different aspects of safety of exercise with comorbid neuropathy are at issue:
(1) Safety of exercise with autonomic neuropathy, (2) Ulcer risk with existing neuropathy,
(3) Fall risk with existing neuropathy.

Safety of exercise with autonomic neuropathy. Existing guidelines are not based on data and are therefore are outside the scope of this chapter. Graham and Lasko-McCarthy and Sigal and colleagues provide further information on this topic (112;173).

Ulcer risk with existing neuropathy. Two studies observed an inverse relationship between physical activity and ulcer incidence (174;175). However, 2 other studies have suggested that abrupt increases in activity may increase the short-term risk of ulceration. Armstrong and colleagues found a significantly greater coefficient of variation in the group with recurrent ulcer (174) and Lemaster and colleagues (175) found a significant unadjusted increased risk of ulcer with increased short-term activity. Ulcer risk was increased with greater intensity and duration of loading pressure on the feet while walking (176;177) possibly showing a clinical benefit to protective diabetic footwear in this population.

Risk of falls with existing neuropathy. Several studies have evaluated the degree to which gait is altered by diabetic neuropathy (suggesting attendant increased fall risk), with one study showing a targeted intervention may improve balance in this population. Dingwell and colleagues as well as other researchers have performed studies showing decreased walking speeds or decreased gait variability (176;178-180) in those with diabetic peripheral neuropathy versus non-diabetic controls. Giacomozzi and colleagues also showed those with diabetic neuropathy and a prior foot ulcer had even greater gait variability than those with neuropathy and no prior ulcer (176). Mueller and colleagues showed that the peak torque generated during plantar flexion and the range of motion of dorsiflexion at the ankle are strongly correlated ($r = 0.78$) and contribute to the power generated from the ankle joint during ambulation (181). These data suggest that decreased ankle dorsiflexion range of motion and/or plantar flexion strength are associated with decreased step length and speed during walking (181). Novak and colleagues (182) reported that 30 individuals with T2D and associated diabetic neuropathy described worse foot pain and walked shorter distances than subjects with T2D without neuropathy and non-diabetic controls, with strong correlation between pain level and walking distance ($r = -0.45$, $P < 0.001$) (182).

The data presented here generally support the pragmatic exercise precautions recommended in clinical practice guidelines (Table G3.A14, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.). Those with **severe** peripheral neuropathy should use non-weight bearing activities to avoid foot ulceration or Charcot joint destruction (112;173), and all individuals with diabetes should use appropriate footwear and inspect their feet daily to reduce injury risk (183).

Diabetic Nephropathy

Four cross-sectional studies (150;152;166;184) and 1 retrospective cohort study (167) have evaluated the impact of physical activity on diabetic nephropathy prevention in subjects with T1D (Table G3.A12). These data are not available in patients with T2D. From these limited data, no firm conclusions may be drawn but they suggest physical activity may prevent diabetic nephropathy. In 2 separate cross-sectional analyses of slightly different subsets of a Finnish population with T1D, less physical activity was associated with greater prevalence of nephropathy (150;152). A significant association was observed between greater leisure-time physical activity and decreased nephropathy in men only, with no increased risk in women with T1D (166). The other 2 observational studies performed showed neither harm nor benefit in prevention of diabetic nephropathy (167;184).

Physical Activity To Treat Diabetic Nephropathy

A pre-post analysis (185) evaluated the effect of 3 weeks of physical activity and low-calorie diet in treating existing nephropathy (Table G3.A13) in subjects with T2D. Although albuminuria was reduced, the dietary intervention and/or associated weight loss may have confounded these results. These data are somewhat promising but inconclusive.

Safety of Physical Activity With Existing Nephropathy

The relevant literature appears to show that exercise does not worsen resting proteinuria (186-188). In a cohort of 373 subjects with T1D, a strong correlation between overnight albumin excretion rate (AER) and post-exercise AER existed ($r = 0.74$, $P < 0.001$), and 52% of subjects had an elevated overnight AER preceding an elevated post-exercise AER (186). In a smaller cross-sectional study, Groop and colleagues (187) showed exercise did not increase protein excretion in 17 subjects newly diagnosed with T1D, but that 17 subjects with long-standing T1D had a significant increase in post-exercise excretion of albumin, β2-microglobulin, Kappa light chains, and IgG independent of whether resting AER was elevated (n=7) or normal (n=10). A small cohort study found no significant difference in time for nephropathy progression in 6 subjects with "good" unrestricted physical activity as compared with 7 subjects with "self-restricted" physical activity (188).

Despite hypothetical adverse effects of increased proteinuria immediately after exercise (189), existing data show no progression of nephropathy with exercise and, in fact, increasing physical activity may decrease existing albuminuria, as described earlier in this section (185;190;191). In the absence of primary data for other safety considerations in those with diabetic nephropathy, a review of these issues is outside the scope of this discussion, although guidelines exist (112;173).

Diabetic Retinopathy

One moderate-sized prospective cohort study (192), and several cross-sectional (150;152;166;184;193) and retrospective (167;194) observational studies have evaluated the impact of physical activity on diabetic retinopathy (Table G3.A12) in T1D. These limited data suggest that physical activity does not influence the risk of developing diabetic retinopathy. The moderately sized cohort study (192) observed no difference in the incidence of retinopathy over 6 years in 606 T1D subjects with respect to current physical activity or historical participation in team sports, in contrast to an earlier cross-sectional analysis (193) in a subset of the same cohort population where a decreased prevalence of retinopathy in women who played team sports (OR 0.46, $P < 0.05$) or who reported current strenuous physical activity (OR 0.34, $P < 0.05$) was previously observed. Two cross-sectional analyses of slightly different subsets of a Finnish population with T1D found no association between physical activity and retinopathy (150;152) despite an association between physical activity and less nephropathy in those same studies (150;152). Of the 4 other cross-sectional studies performed, none showed any benefit or harm of physical activity in the prevention of diabetic retinopathy (166;167;184;194).

Treatment of Diabetic Retinopathy

A large cohort study reported no impact of self-reported current or historical physical activity measurements on retinopathy in a large cohort of T1D subjects with both non-proliferative and proliferative retinopathy at baseline measurement (192).

Safety of Physical Activity With Existing Diabetic Retinopathy

Although existing data raise concerns about the plausible causality of exercise-induced vitreous hemorrhages individuals with diabetic retinopathy, existing data have not conclusively shown a risk of moderate-intensity exercise in those with this condition (195).

The 2 prospective studies evaluating the safety of exercise in humans with existing retinopathy have not shown an increased risk of retinopathy progression or of vitreous hemorrhage in this population. The prospective cohort study analysis by Cruickshanks and colleagues showed no risk of worsened retinopathy in those with T1D who were more physically active over a 6-year period as compared with their more sedentary counterparts, including a very small subset of self-described weight lifters (192). A pre-post exercise intervention study in 30 subjects with T1D or T2D and existing proliferative diabetic retinopathy (90% or greater) or diabetic macular edema observed no newly documented vitreous hemorrhages attributable to a 12-week supervised exercise training program, although the study was under-powered to definitively determine vitreous hemorrhage risk (196).

Given the preceding evidence, clinical providers have generally recommended moderate-intensity exercise but advised against vigorous exercise regimens for those with proliferative retinopathy (112;173;183;197) and severe nonproliferative retinopathy (112) due to the theoretical (yet unproven) increased risk for vitreous hemorrhage and retinal detachments with vigorous exercise.

Cardiovascular Safety of Physical Activity With Existing Microvascular Complications

Despite a lack of studies evaluating this practice, the most recent published standards of care suggest that diabetic subjects with more than a 10% 10-year risk for CV disease by the United Kingdom Prospective Diabetes Study risk calculator (198) should **consider** exercise stress testing to screen for latent ischemia before initiating vigorous aerobic exercise regimens that exceed the “demands of everyday living” (199).

Question 6: Do Physical Activity and Exercise Have a Role In Preventing Gestational Diabetes?

Conclusions

Although no RCTs have been performed to demonstrate that physical activity can prevent gestational diabetes (GDM), data from observational studies support that concept. Available studies suggest that approximately 30 minutes per day of moderate-intensity physical activity is likely a sufficient dose to decrease the GDM risk (200). However, this suggestion is based on relatively few studies, and further studies should directly address the issue of dose-response.

Introduction

Gestational diabetes is defined as diabetes first identified during pregnancy. Overall, prevalence rates of GDM have increased from 1.9% in 1989-1990 to 4.2% in 2003-2004, a relative increase of 122% (201). The prevalence of GDM is 17% in obese women, and overweight women have a significantly greater risk of developing GDM than do non-overweight women (202). It is estimated that up to 60% of women with GDM will develop T2D within 4 years of delivery (203). GDM can give rise to many adverse outcomes both to mother and infant. It is associated with a greater likelihood of Caesarean section deliveries and other birth complications (204). Women with GDM also are more likely to have a difficult labor and delivery. Babies of women with GDM are at increased risk of obesity and diabetes later in life as well as other comorbid conditions at birth (205).

Given that women who develop GDM are at highly increased risk of developing T2D, understanding how to prevent and treat GDM is very important. The role of physical activity in preventing and treating GDM has not been as well studied as for T2D. Indeed, no RCTs have assessed whether GDM can be prevented by regular physical activity. However, observational epidemiologic studies suggest overall that this may be the case (Table G3.A15, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.).

Rationale

Data From Observational, Epidemiological Studies

Several studies have shown that physical activity is associated with a significantly reduced risk of GDM (200). These studies reported that increased levels of physical activity (assessed by questionnaire) before pregnancy or during the first 20 weeks of pregnancy was associated with reductions in risk of GDM. Overall the reduction in risk is about 50% when active women are compared to inactive women.

Dose-Response Data

No RCTs have evaluated prospectively whether physical activity can prevent GDM or what doses might be effective for such a response. Such trials would be of great value to establish the role of exercise and physical activity in GDM. Available studies suggest that approximately 30 minutes per day of moderate intensity physical activity is likely a sufficient dose to decrease the GDM risk (200). However, this suggestion is based on relatively few studies, and further studies should directly address the issue of dose-response.

Overall Summary and Conclusions

In summary, physical activity and exercise play a key role in preventing and treating metabolic syndrome and T2D. The evidence for T2D are the clearest because RCTs have been conducted to corroborate the findings of many observational trials, although, as mentioned previously, 2 of the 3 RCTs combined physical activity and diet in their lifestyle intervention. (The post-hoc findings on effects of physical activity in the absence of weight change, although consistent and strong, are therefore not considerd strong RCT data but rather are equivalent to the quality of prospective cohort study data.) The role of physical activity and exercise in treating T1D is still being established. Current evidence suggests that benefits are likely, perhaps most of all in the area of reducing mortality, CVD risk factors, and microvascular complications. For both T1D and T2D, physical activity may prevent the development of diabetic neuropathy and diabetic nephropathy. Finally, it appears likely that physical activity and exercise may help prevent and treat gestational diabetes although more research is needed to establish these findings. The amount of exercise that appears to be the most well accepted and documented across the conditions included in this section to date is 30 minutes of moderate physical activity 5 days per week. However, it is clear that benefits are obtained with even lower volumes of physical activity. Walking is a beneficial form of physical activity and has been especially well documented as effective in T2D (where it has been most extensively studied). In the next section, the extensive research needs for further study in the area of Metabolic Health are documented.

Research Needs

Although a considerable body of literature exists on the role of physical activity in promoting and maintaining metabolic health, a number of questions remain unanswered and require additional research:

- Available data indicate that regular physical activity is associated with reduced risk of metabolic syndrome. However, it is not clear whether physical activity and exercise can be used in treating or reversing metabolic syndrome, and additional studies will help to clarify this issue.

- Research is needed in diverse populations to determine whether the effects of physical activity across the range of metabolic health issues, including metabolic syndrome, T2D, T1D, and gestational diabetes, differ with race and ethnicity.

- Further examination of the effects of physical activity on metabolic syndrome and T2D also is warranted to determine whether and how its effect differ in youth and adults.

- Additional research evaluating dose-response patterns of exercise in preventing diabetes and cardiovascular outcomes in diabetes would make a valuable contribution to the metabolic health literature.

- RCTs are needed to examine the effects of exercise on treating T1D in children and adults. Good cardiovascular outcome data in response to physical activity in T1D is lacking and could potentially be obtained in adult-onset T1D.

- Clinical studies in post-exercise hypoglycemia are needed to further study the intermittent high-intensity exercise approach to prevention and to compare extra carbohydrate versus lower insulin dosing approaches to treating T2D.

- Research is needed on several issues related to gestational diabetes. For example, RCTs are needed to determine whether physical activity can prevent gestational diabetes. It also would be useful to have additional dose-response data on the role of exercise and physical activity in treating gestational diabetes.

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Part G. Section 4: Energy Balance

Introduction

Overweight and obesity are linked to increased risk of morbidity from hypertension, dyslipidemia, type 2 diabetes, coronary heart disease, stroke, gallbladder disease, osteoarthritis, sleep apnea and respiratory problems, and endometrial, postmenopausal breast, prostate, and other cancers (1;2). In addition, obesity is associated with excess overall mortality (3). Unfortunately, the prevalence of overweight and obesity has increased dramatically over the past 20 years in the United States to 70.8% and 31.1% for adult men, and 61.8% and 33.2% for adult women, respectively (4). This increase has been attributed to changes in environment and lifestyle factors because the escalating prevalence has been occurring in a constant genetic milieu. The focus in this chapter is on the role that physical activity plays in energy balance.

Review of the Science

Overview of Questions Addressed

This chapter addresses 5 major questions related to physical activity and energy balance.

1. How much physical activity is needed for weight stability and weight loss?
2. How much physical activity is needed to prevent weight regain in previously overweight individuals?
3. What is the effect of physical activity on body composition parameters (e.g., waist circumference, intra-abdominal fat, abdominal obesity, total body fat) that are related specifically to metabolic disorders?
4. What effects do sex and age have on the role of physical activity in energy balance?
5. How do the physical activity requirements for weight maintenance differ across racial/ethnic and socioeconomic groups?

Data Sources and Process Used to Answer Questions

The Energy Balance subcommittee used the *Physical Activity Guidelines for Americans* Scientific Database as its primary source for each question (see ***Part F. Scientific Literature Search Methodology,*** for a complete description of the Database). It also used other databases, reviews, and meta-analyses to obtain evidence bearing on each question. Specific search strategies are described for each question.

Caveats

Four points need to be mentioned at the outset of this chapter on physical activity and energy balance. First, in contrast to outcomes addressed in other chapters, in which physical activity can be discussed as the primary variable affecting the outcome, achieving energy balance is dependent on both energy intake and energy expenditure. With the availability of inexpensive and easily accessed high-calorie, highly palatable foods, it is far easier to increase energy intake than to increase energy expenditure in our society. In support, the 2005 Dietary Guidelines Advisory Committee Report (5) indicated that most Americans are consuming energy in excess of energy needs, and it is not likely to change in the near future. Consequently, final recommendations related to the level of physical activity needed for weight maintenance, weight loss, or prevention of weight regain after weight loss must consider energy intake issues as well.

Second, when a caloric deficit induced by exercise is compared with an equivalent caloric deficit created by a reduction in caloric intake, there is little or no difference in weight loss (6). However, in many weight loss studies, the proportion of the caloric deficit due to physical activity is only a small fraction of the overall caloric deficit, and consequently, the contribution that physical activity makes to weight loss is relatively small. This must be remembered as we address the role of physical activity **alone** on weight-related issues.

Third, secular trends have increased the use of automation and labor-saving devices on the job, at home and in the community and increased passive leisure-time physical activity (e.g., TV/VCR, computer use). These trends influence the amount of physical activity needed to achieve energy balance.

Finally, if we did not have an overweight and obesity problem in our society, we would still need a physical activity recommendation to maintain health and prevent disease. That simple message is lost on many who focus solely on the role of physical activity in preventing overweight and obesity. Consequently, the level of physical activity needed to maintain health and prevent disease is the baseline for any physical activity recommendation for energy balance.

Question 1: How Much Physical Activity Is Needed for Weight Stability and Weight Loss?

Conclusions

All study designs provide clear evidence of a dose-response relation between physical activity and weight loss. However, few data are available on weight stability over the long term. Available data on weight stability are from short-term clinical trials. Based on these trials, a dose of physical activity in the range of 13 to 26 MET-hours per week resulted in a modest 1% to 3% weight loss, consistent with weight stability over time (7-9). Thirteen MET-hours per week is equivalent to walking at a 4 mile per hour pace for 150 minutes per week or jogging at a 6 mile per hour pace for 75 minutes per week. The magnitude of weight loss resulting from studies of resistance exercise is typically less than 1 kilogram (2.2 pounds). However, this result may be affected by the relatively short duration of these studies and gains in fat-free mass that accompany such interventions. In contrast, it is clear that if one wants to achieve weight loss (i.e., more than 5% decrease in body weight), a dietary intervention also is needed. The dietary intervention could include either a maintenance of baseline caloric intake, or a reduction in caloric intake to accompany the physical activity intervention. The magnitude of change in weight due to physical activity is additive to that associated with caloric restriction.

Definitions

To aid in the study of patterns of weight change, the scientific literature has operationally defined the concept of weight stability. St. Jeor and colleagues (10) define weight stability as a change of 2.3 kilograms (5 pounds) or less of initial body weight. In this study, participants' weights were monitored over a period of time using this criterion. It was determined that 62%, 52%, 49%, and 46% of participants were classified as maintaining their body weight at 1, 2, 3, and 4 years of follow-up, respectively. The Pound of Prevention Study also defined weight maintenance as a change of 2.3 kilograms (5 pounds) or less (11) of initial body weight. When examined over a 3-year period, 40% of men and 38% of women were classified as "maintainers," with a mean weight change of 0.3 kilograms (0.7 pounds) and 0.2 kilograms (0.4 pounds), respectively. Moreover, across the entire sample of 957 individuals, the mean weight gain over a 3-year period was 1.7 kilograms (3.7 pounds) for men and 1.8 kilograms (4 pounds) for women. This would suggest that the mean weight gain across the population may be approximately 0.6 kilograms (1.3 pounds) per year.

More recently, Stevens and colleagues (12) have recommended that weight maintenance be defined as less than a 3% change in body weight. Moreover, they recommended that a change in body weight of 3% to less than 5% of initial weight be considered as small fluctuations in body weight, and a change of 5% or more of body weight be considered clinically significant. Considering these standards, an obese individual weighing 91 kilograms (200 pounds) would need to reduce body weight by 4.5 kilograms (10 pounds) to have a significant weight loss, and a weight change of 2.7 kilograms (6 pounds) would be considered weight stability. These standards should be considered when evaluating the effect of physical activity on body weight change to determine whether various doses and modes of physical activity result in weight stability or clinically relevant weight loss.

Rationale

A search of the *Physical Activity Guidelines for Americans* Scientific Database identified 126 research articles on the effect of physical activity on weight loss and weight stability. Additionally, pertinent reviews available through a MEDLINE search were considered.

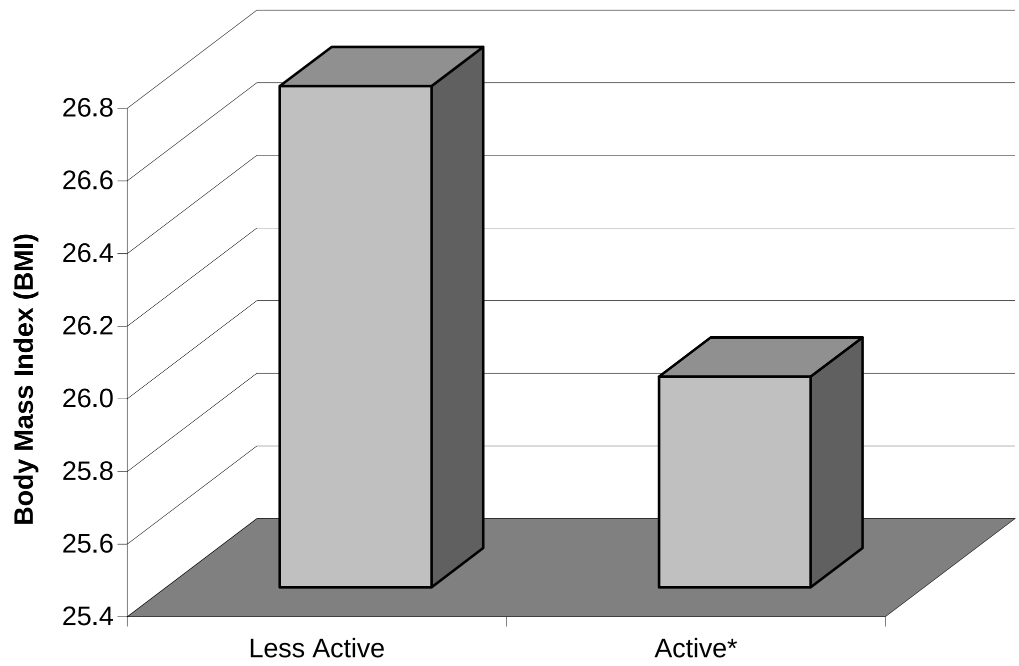
Cross-Sectional Studies

Twenty-four cross-sectional studies were identified that examined the association between physical activity and body weight. Of these 24 studies, 23 reported results suggesting an inverse relationship between physical activity and body weight and/or body mass index (BMI) (13-35). These studies tended to illustrate a dose-response relationship between physical activity and body weight or BMI. For example, Giovannucci and colleagues (14) reported that when 0.9, 4.8, 11.3, 22.6, and 46.8 MET-hours per week were used to define quintiles of physical activity, corresponding BMI values were 25.4, 25.3, 25.1, 24.7, and 24.4 kg/m^2, respectively. More recently, Kavouras and colleagues (15) reported that individuals participating in physical activity that is consistent with the current consensus public health recommendations of at least 30 minutes per day on 5 days a week had a significantly lower BMI (25.9 kg/m^2) when compared to the BMI (26.7 kg/m^2) of less active individuals (Figure G4.1). Thus, based on these findings, it appears that levels of physical activity that are consistent with a range of 30 to 60 minutes per day on at least 5 days per week (150 to 300 minutes per week) is sufficient to maintain and/or significantly reduce body weight.

Prospective Studies

Nine prospective studies were identified that reported on the benefits of physical activity to prevent weight gain and/or result in weight loss (36-44). Three studies, which had a follow-up period of 1 to 3 years, all reported a favorable association between physical activity and weight-related outcomes (36;37;39). The remaining 6 studies, which had a follow-up period of 6.5 years or greater, also reported a favorable association between physical activity and weight-related outcomes (38;40-44). Berk and colleagues (43) found that individuals who initially reported less than 60 minutes per week of physical activity and increased to 134 minutes per week of physical activity had an increase in BMI of 0.4 kg/m^2 across a 16-year follow-up period, but this was not significantly different from the 0.9kg/m^2 increase observed for individuals who remained sedentary (less than 60 minutes per week) at both assessment periods. These data suggest that less than 150 minutes per week of physical activity will result in a non-significant blunting of weight gain compared to individuals who remain sedentary. However, individuals who were classified as active at both assessment periods were participating in 261 minutes per week of physical activity, and had a significantly smaller change in BMI compared to individuals who were initially active (more than 60 minutes per week) at baseline but became inactive at follow-up (less than 60 minutes per week). This supports the need to maintain a physically activity lifestyle to manage body weight long-term.

Figure G4.1. Differences in Body Mass Index Due to Level of Physical Activity



*Active is defined as the consensus public health recommendation for physical activity (3 or more days per week of 20 minutes per day at vigorous intensity or 5 or more days per week of 30 minutes per day at moderate intensity).
Source: Adapted from Kavouras and colleagues, 2007 (15).

Figure G4.1. Data Points

	Less Active	Active*
BMI	26.7	25.9

Randomized Trials

Endurance Exercise

Twenty studies were identified that examined the effect of endurance exercise on body weight. However, 7 studies were not reviewed due to the intent of the study to focus on marathon training, a dietary intervention to counter or enhance the weight loss effects of exercise, the inclusion of only subjects with serious psychiatric disabilities, the lack of a consistent training paradigm across the observation period, or the exercise volume not expressed in as minutes per week. The remaining 13 studies were reviewed in greater detail. Twelve used a randomized design, although 3 of them did not have a control group and/or the physical activity was in addition to a dietary intervention (45-47), and 1 used a non-randomized design to examine the effect of physical activity but did not include a comparison group (48). In addition, the primary purpose of 5 of the studies was on something other than weight loss (49-53). The remaining 4 studies (7-9;54) had sufficient statistical power to evaluate the effect of physical activity on body weight and body composition.

These studies ranged in duration from 8 to 16 months, and physical activity level ranged from 180 minutes of moderate-intensity physical activity per week to 360 minutes of moderate- to vigorous-intensity physical activity per week. In addition, one study (9) evaluated 3 levels of physical activity, and 2 (7;8) established, post hoc, tertiles of physical activity participation (adherence) based on activity logs and/or pedometer records to evaluate a dose-response pattern. Typical weight losses were 1 to 3 kilograms (2.2 to 6.6 pounds), which corresponded to less than 3% change in body weight, but evidence of a dose-response relationship was clear, with those doing the greatest amount of physical activity achieving weight losses of 4% to 6% (the latter associated with an energy expenditure of 668 kcal per session, 5 days per week). A dose of physical activity in the range of 13 to 26 MET-hours per week resulted in a modest 1% to 3% weight loss, consistent with weight stability over time.

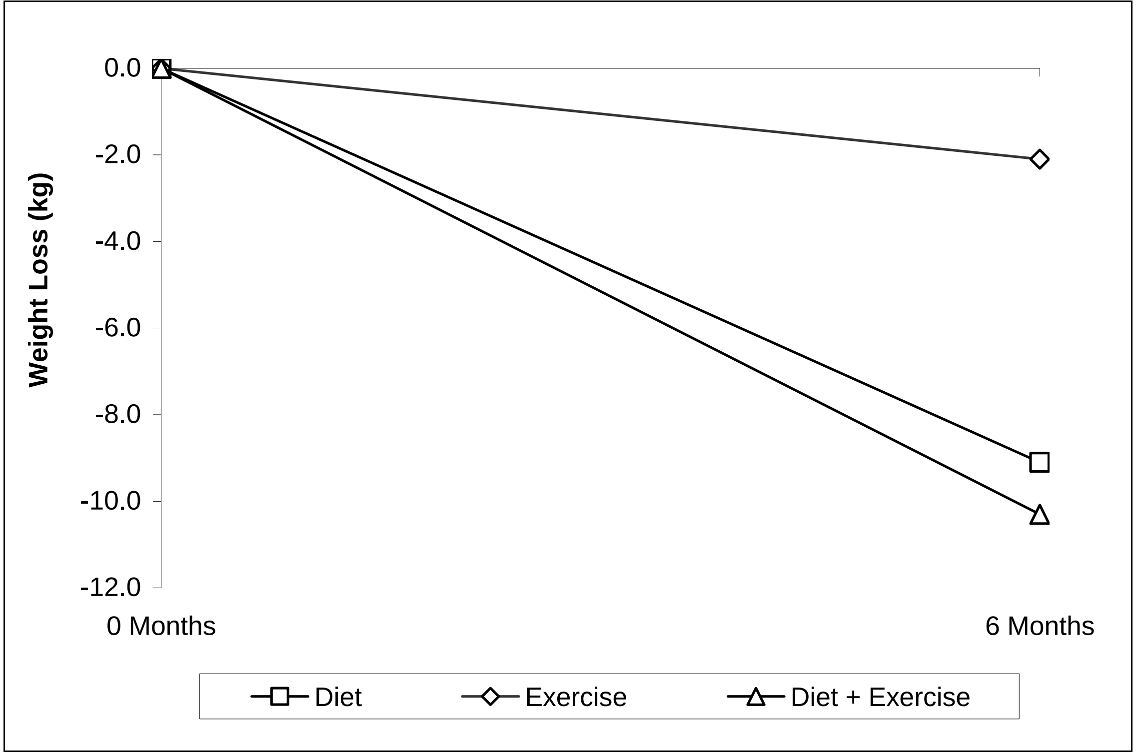
Resistance Exercise

An alternative form of physical activity is resistance exercise. Ten studies were reviewed that examined the impact of this form of exercise on change in body weight, and all of these studies showed a modest reduction (less than 1 kilogram) or a non-significant change in body weight (55-64). This finding of a modest impact of resistance exercise on body weight was confirmed in a literature review (65). A potential explanation for this lack of a reduction in body weight is that many of these studies reported an increase in fat-free mass resulting from resistance exercise training, which resulted in a reduction in percent body fat, but did not change absolute body weight or fat mass. Thus, changes in body composition may be a desirable outcome to examine when determining the effect of resistance exercise on body weight parameters. However, the lack of a sufficient dose of physical activity to elicit a significant energy deficit may also explain these findings, as many of these studies were relatively short in duration and included only 2 to 3 days per week of resistance exercise.

Five studies from the *Physical Activity Guidelines for Americans* Scientific Database examined the combination of endurance and resistance exercise on change in body weight. Two studies used randomized designs to assign participants to a physical activity group or a control group (66;67), 1 used a randomized cross-over design involving 8 weeks of physical activity and 8 weeks of no physical activity (68), and 2 examined the effect of physical activity but did not include a control group (69;70). Four of these studies reported no effect of combined endurance plus resistance exercise on change in body weight (66-69), and 1 study that did not include a control group (70) reported a significant effect. A potential limitation of these studies is that they ranged from 8 to 10 weeks in duration, which may have been too short a time to significantly affect body weight.

In general, regular participation in moderate-to-vigorous physical activity is associated with weight maintenance over time. In contrast, it is clear that if one wants to achieve clinically relevant weight loss (a decrease of 5% or more in body weight), a dietary intervention is usually needed. This is shown clearly in Figure G4.2, adapted from Wing, 1999 (71).

Figure G4.2. Weight Loss Related to a Diet Intervention, an Exercise Intervention, and a Diet + Exercise Intervention



Source: Adapted from Wing, 1999 (71)

Figure G4.2. Data Points—Weight Loss in kg

	0 Months	6 Months
Diet	0	-9.1
Exercise	0	-2.1
Diet + Exercise	0	-10.3

The magnitude of weight loss due to physical activity is additive to caloric restriction, but physical activity is generally insufficient by itself to bring about clinically significant weight loss. Consistent with this, McTiernan and colleagues (8) estimated that the physical activity intervention in their study should have produced a weight loss of 7.8 kilograms, rather than the 1.4 kilograms (women) and 1.8 kilograms (men) observed, **if caloric intake had remained stable.** Further, studies in which the caloric intake was held constant (by design) from baseline showed that the weight loss associated with the physical activity intervention was what one would predict from the physical activity energy expenditure (6). Consequently, the addition of a dietary restraint **to not increase caloric intake** may have resulted in clinically significant weight loss, rather than just weight stability with the physical activity intervention mentioned above. The magnitude of weight loss reported in these studies is consistent with earlier reviews on this topic by Wing (71) and the Expert Panel of Clinical Guidelines for the Treatment of Obesity (1).

Question 2. How Much Physical Activity Is Needed to Prevent Weight Regain in Previously Overweight Individuals?

Conclusions

Most of the available literature indicates that "more is better" when it comes to the amount of physical activity needed to prevent weight regain following weight loss. However, the literature has some considerable shortcomings regarding the appropriate research design needed to directly address this question. Given these limitations, the estimated gross energy expenditure needed to achieve weight maintenance following substantial weight loss is about 31 kilocalories per kilogram week or 4.4 $kcal \cdot kg^{-1} \cdot d^{-1}$, which is equivalent to walking 54 minutes per day at a 4 mile per hour pace, walking 80 minutes per day at a 3 mile per hour pace, or jogging 26 minutes per day at a 6 mile per hour pace (72-74).

Rationale

Initial references were obtained with a search of the *Physical Activity Guidelines for Americans* Scientific Database. Key words included adults, exercise, physical activity, obesity, adiposity, weight, and BMI. Eight systematic reviews or meta-analyses also were reviewed for pertinent references. Studies that investigated special populations (e.g., physically disabled), included individuals with a disease known to affect weight (e.g., cancer), or weight loss drugs, were excluded. To be included, studies had to target a period of weight loss followed by a period of weight maintenance using physical activity as the strategy for preventing weight regain.

Eight randomized trials met the above criteria and were used for this review. Of the eight studies, only three had a design in which participants were randomized after weight loss and only two used a control group. Three observational or prospective cohort studies were identified that met the above criteria and were used for this review. Four position papers or reports also were used as references.

It is generally accepted that individuals can lose weight but most cannot maintain significant weight loss. Because it has an energy equivalent, physical activity is universally promoted as a necessary component of strategies to maintain weight loss (1;75;76). Indeed, physical activity is often cited as the best predictor of weight maintenance after weight loss (77;78). A systematic review of physical activity to prevent weight regain subsequent to weight loss was completed by Fogelholm and Kukkonen-Harjula (79). The majority of studies included in this review were observational studies and studies of individuals who were randomized at baseline to exercise or no exercise, or to different levels of physical activity. Follow-up varied from several months to several years and generally showed that individuals who engaged in exercise experienced less regain than those individuals who did not, and those individuals who engaged in greater amounts of physical activity experienced less regain than those who did more moderate levels. Only 3 studies used a design in which individuals were randomized to physical activity after weight loss (80-82), and the results were inconsistent, showing that physical activity had an indifferent, negative, or positive effect on prevention of weight regain.

Despite the accepted concept that physical activity is necessary for successful weight maintenance after weight loss, the amount that is needed remains uncertain. The 1995 Centers for Disease Control/American College of Sports Medicine (CDC/ACSM) recommendations for physical activity specified the accumulation of 30 minutes of moderate-intensity physical activity for most days of the week (83). These guidelines were provided for health promotion and disease prevention. However, they were widely interpreted to also be useful for weight management. Minimum levels of 150 minutes per week (30 minutes per day, 5 days a week) of moderate-intensity physical activity were also recommended by the ACSM Position Stand for “Appropriate Intervention Strategies for Weight Loss and Prevention of Weight Regain for Adults” (75). However, recent evidence suggests that greater levels of physical activity may be necessary to prevent weight regain after weight loss. For example, individuals in the National Weight Control Registry who have maintained weight loss have shown levels of energy expenditure equivalent to walking about 28 miles a week (77). Schoeller and colleagues (74) used doubly-labeled water to study women who recently lost 23±9 kilograms of weight in order to estimate the energy expenditure needed to prevent weight regain. Retrospective analyses of these data were performed to determine the level of physical activity that provided maximum differentiation between gainers and maintainers. Based on these analyses, it was determined that individuals would need to expend about 4.4 kilocalories per kilogram per day in physical activity (which is equivalent to about 80 minutes per day of moderate-intensity physical activity or 35 minutes per day of vigorous physical activity) to prevent weight regain.

Jakicic and colleagues (73;84) and Andersen and colleagues (85) provided data from randomized trials showing that individuals who performed large amounts of physical activity maintained weight loss better at follow-up of 18 months, 12 months, and 12 months, respectively, than did those doing smaller amounts of physical activity. In particular, Jakicic and colleagues (73;84) showed very little weight regain in individuals who performed more than 200 minutes per week of moderate-intensity physical activity. Ewbank and colleagues (72) also found similar results 2 years after weight loss by very-low-energy diet. Retrospectively grouping participants by levels of self-reported physical activity, individuals who reported greater levels (i.e., walking about 16 miles per week,) had significantly less weight regain than individuals reporting less physical activity per week (4.8 to 9.1 miles per week). However, it is important to note that individuals in all 3 studies above were grouped into physical activity categories retrospectively and were not randomly assigned to those groups after weight loss. Thus, the amount of physical activity was self-selected and therefore does not provide clear evidence for the amount needed to prevent weight regain.

To explore the effects of levels of physical activity greater than those normally recommended in weight management programs, Jeffery and colleagues (86), targeted energy expenditures of 1,000 kilocalories per week and 2,500 kilocalories week for 18 months in 2 groups of participants; these levels were randomly assigned at baseline. The actual reported energy expenditure at 18 months was 1,629 ± 1,483 and 2,317 ± 1,854 kilocalories per week for the 1,000 and 2,500 kilocalories per week groups, respectively. At 6 months, weight loss did not differ between the groups, but there were significant differences at 12 and 18 months (weight maintenance) follow-up, with the 2,500 kilocalories per week group showing significantly greater weight losses (6.7 ± 8.1 kilograms versus 4.1 ± 8.3 kilograms). The energy equivalent for walking for the 2,500 kilocalories per week group and 1,000 kilocalories per week group was about 3.3 miles per day and about 2.3 miles day, respectively. This study showed that greater levels of physical activity resulted in significantly lower levels of weight regain. However, the results must be interpreted with caution, as the percentage of individuals meeting the targeted energy expenditure varied greatly, and the behavioral interventions were not equal.

In general, large volumes of physical activity are needed to prevent weight regain in those who have lost a great deal of weight. Studies by Ewbank and colleagues (72), Jakicic and colleagues (73), and Schoeller and colleagues (74) indicate that the volume of physical activity needed for that purpose is approximately 31 MET-hours per week or 4.4 MET-hours per day.

Question 3. What Is the Effect of Physical Activity on Body Composition Parameters (e.g., Waist Circumference, Intra-Abdominal Fat, Abdominal Adiposity, Total Body Fat) That Are Specifically Related to Metabolic Disorders?

Conclusions

A dose-response relation exists between volume of physical activity and decreases in total and abdominal adiposity in overweight and obese individuals. In the absence of coincident caloric restriction, aerobic physical activity in the range of 13 to 26 MET-hours per week results in decreases in total and abdominal adiposity that are consistent with improved metabolic function. Thirteen MET-hours per week is equivalent to walking at a 4 mile per hour pace for 150 minutes per week or jogging at a 6 mile per hour pace for 75 minutes per week (7-9). However, larger volumes of physical activity (e.g., 42 MET-hours per week) result in decreases in intra-abdominal adipose tissue that are 3 to 4 times those seen with 13 to 26 MET-hours per week, even without weight loss. The evidence thus far suggests that abdominal fat loss with increased physical activity is proportional to overall fat loss.

Definitions

The obesity phenotype that conveys the greatest health risk of metabolic disorders, such as the metabolic syndrome and type 2 diabetes, is one that favors an accumulation of adipose tissue in the abdominal region. Regular physical activity is recognized as an effective method of preventing excessive weight and fat gain throughout adulthood, and although physical activity is commonly prescribed to reduce overall obesity, the influence of exercise-induced weight loss on abdominal adiposity is not clear. Abdominal adiposity is characterized several ways in the scientific literature. Modern imaging techniques such as MRI, DXA, and CT provide highly-precise quantification of total body fat content (expressed in relative [%] or absolute [kilogram] terms), as well as specific measures of abdominal fat, such as the subcutaneous and visceral (intra-abdominal) fat areas (cm^2). Although less precise than the imaging measures, the waist circumference (measured in centimeters and usually defined at the level of the lowest rib) is the most widely-used anthropometric measure of abdominal adiposity and therefore has the most clinical utility of all these measures.

Rationale

The *Physical Activity Guidelines for Americans* Scientific Database was accessed using the following delineation terms: 1) **population sub-group:** adults/older adults; 2) **study design:** randomized controlled trials (RCTs); longitudinal experimental studies (before/after); and prospective observational studies; and 3) **health outcomes:** adiposity measures (e.g., total fat, percent fat, abdominal fat area [visceral and subcutaneous], waist circumference) related specifically to metabolic disorders. Evidence obtained using the Scientific Database was supplemented with recently-published scientific papers and review articles.

Favorable body composition changes (reduced fat mass and increased lean mass) occur with the adoption of regular physical activity — even among individuals aged 75 years and older, and evidence suggests that current activity is more protective than past activity (87;88). What is not clear at this time is the amount and type of activity necessary to result in meaningful alterations in abdominal fat, which in turn can preserve or improve metabolic function. Unfortunately, few large-scale RCTs have been directed toward this question. The data that do exist are from relatively small RCTs and controlled intervention studies. Nonetheless, these studies paint a consistent picture of energy expenditure requirements for minimizing fat gain and/or reducing excess total and abdominal fat.

Several RCTs and controlled interventions report the benefits of moderate- to vigorous-intensity aerobic exercise to overall improvements in body weight, body fat, and lean mass in middle-aged and older adults (7;8;89-93). The data are equivocal, however, with regard to the ability to significantly alter regional distribution of body fat with endurance training (7-9;54;91;93-95). In general, aerobic exercise, without dieting, appears to have a beneficial effect on overall and abdominal adiposity. However, the exercise dose necessary to result in these alterations is rather high. In Irwin and colleagues (7), 176 minutes per week of moderate- to vigorous-intensity physical activity performed over 12 months resulted in a reduction in subcutaneous fat and intra-abdominal fat of 5.4% and 5.8%, respectively, with the impact being even larger when contrasted with the control group. In addition, McTiernan and colleagues (8) used a higher volume/longer duration aerobic exercise regimen (60 minutes or more of moderate- to vigorous-intensity physical activity on 6 days per week) over 12 months of training and also reported modest decreases in the subcutaneous abdominal fat (5% in women and 11% in men) and intra-abdominal fat (6% in women and 8% in men) depots and in the waist circumference (2% in women and 3% in men). Data from the Studies of Targeted Risk Reduction Interventions through Defined Exercise (STRRIDE) show that the highest amount of exercise performed (equivalent of jogging approximately 20 miles per week) over 8 months resulted in, at best, a 7% decrease in visceral and subcutaneous fat in men and women aged 40 to 65 years (9). Ross and colleagues (93) report an 18% reduction in total fat and a 20% reduction in abdominal fat among non-dieting abdominally-obese women who exercised every day for about 60 minutes (or 500 kilocalorie expenditure) for 14 weeks. Together, these findings (7-9;93) and others (6) support the contention that in the absence of coincident caloric restriction, aerobic physical activity in the range of 13 to 26 kilocalories per kilogram per week results in decreases in total and abdominal adiposity that are consistent with improved metabolic function. However, as mentioned above, when more physical activity is done per week (e.g., 42 MET-hours per week), decreases in intra-abdominal adipose tissue approach 3 to 4 times the level seen with 13 to 26 MET-hours per week, even without weight loss (93).

A recent study employing 45 minutes of resistance exercise training twice weekly also reports small, yet favorable changes in total and abdominal fat (56) in middle-age and older adults, but not in younger, non-obese women (96). In a 2-year study of resistance training in overweight and obese premenopausal women, Schmitz and colleagues (56) report a 4% decrease in total fat in the exercise group versus a negligible change in the control group ($P<0.01$). Interestingly, intra-abdominal fat increased over 2 years by 7% in the exercise group and by 21% in the control group, underscoring the benefits of resistance training (without caloric restriction) in at least minimizing intra-abdominal fat gain in middle-aged women. The benefits of resistance training may be most noticeable among obese and older populations, who typically have the greatest amount of abdominal fat.

Generally, short-term (less than 6 months) exercise interventions will have a positive effect on body composition. However, the magnitude of these alterations in body fat or lean mass may be of limited biological significance (48). Studies that employ moderate- to vigorous-intensity aerobic exercise of at least 55-75% VO_{2peak} (4.5-6 METs), on most days of the week (i.e., 4 or more days), over intervention periods of at least 9 months, report the most significant changes in body composition (7-9;91;93). In general, the amount of adiposity present in study subjects at baseline will affect the amount of fat lost with a given intervention. Indeed, studies employing overweight or obese subjects (7;8;56;92;93) report greater improvements in body composition than those studies using subjects of normal weight (48;96). Also important is the dose-response relation highlighted by Ross and colleagues (93) between exercise-induced weight loss and fat loss — that is, greater total weight loss will result in greater fat loss (7;93). Nonetheless, Ross and colleagues (93) report that, even without coincident weight loss, 60 minutes per day of vigorous-intensity exercise (approximately 500 kilocalories per day) on 7 days per week still resulted in statistically significant reductions in total (7%), abdominal (10%), and intra-abdominal (18%) fat in abdominally-obese premenopausal women.

Overall, regular participation in aerobic physical activity causes decreases in both total and abdominal adiposity, changes that are consistent with improved metabolic function. The greater the volume of physical activity, the larger the change in adiposity.

Question 4: What Effects Do Sex and Age Have on the Role of Physical Activity in Energy Balance?

Conclusions

Some evidence indicates that the amount of physical activity needed to maintain a constant weight differs between men and women and increases with age. This may be due to a number of physiologic and behavioral factors that also vary by sex and by age. However, the evidence is not sufficient to recommend differential physical activity prescriptions based on sex or on age alone.

Rationale

The *Physical Activity Guidelines for Americans* Scientific Database was accessed using the following delineation terms: 1) **population sub-group:** adults/older adults; 2) **study design:** randomized controlled trials, longitudinal experimental studies (before/after), prospective observational studies, and cross-sectional studies; 3) **health outcomes:** body weight; and 4) **search term:** aging, age, gender, men, women. Studies identified using the Scientific Database were supplemented by recently-published or in press scientific papers and review articles. Findings presented here were limited to studies having a forward study design (i.e., prospective observational and/or longitudinal experimental studies) with adequate statistical power to distinguish moderate effect sizes from chance alone.

Sex

The prevalence of obesity is higher among women compared with men, particularly among women from ethnic minority groups (4;97). Although women report less physical activity than men, it is not clear whether this is actually so, or whether it is a consequence of measurement error resulting from the low sensitivity of traditional physical activity surveys (83;98;99). In any case, potential sex differences in the influence of physical activity on weight stability are important to consider in maximizing the utility of future public health guidelines.

Cross-sectional and longitudinal epidemiologic studies generally have demonstrated inverse associations between physical activity and weight gain in both men and women (e.g., 100-105). Dose-response relationships have been somewhat less consistent in women than in men. However, as stated previously, this may be attributable to measurement error associated with self-reported data (100;106). Indeed, objective measurements of energy expenditure (e.g., doubly-labeled water) have either stronger inverse associations in men than in women or no biological sex differences in response to different amounts of physical activity (107). The few intervention studies that included both men and women (along with sex-specific analyses) report weight or fat losses only in men (107), no change in either sex (67), or similar changes in both men and women (e.g., 8;58;89;108;109).

It is likely that differences in findings among these intervention studies reflect dissimilarities among study protocols. However, even within particular study samples, observed sex differences in weight loss responses to exercise can be attributed to a number of factors. For instance, several highly controlled laboratory-based intervention studies have noted that women are more resistant to weight loss or may require greater energy expenditure compared with men to maintain a healthy body weight (54;100;107). Indeed, this suggests that a similar absolute energy expenditure (e.g., 1,200 kilocalories per week) may not yield the same results in men and women. This may be due to a greater proportion of less lipolytically responsive gluteofemoral adipose tissue in younger and middle-aged women than in men of the same age. Animal studies also have observed a sex dimorphism in the control of energy homeostasis that might be attributed to a differential interaction between adiposity hormones and food intake control systems in the brain (110;111). These biological sex differences in responsiveness to weight change may be difficult to discern in large community-based interventions or at the population level, however, due to measured or unmeasured sex differences in: 1) how a similar level of physical activity is performed (walking vs. water aerobics vs. running); 2) adherence to a given exercise prescription; or 3) dietary intake. Because a number of other physiological (body mass, peak aerobic capacity) or behavioral factors (cigarette smoking, drinking, hormone replacement therapy) also may vary between men and women, studies that measure sex differences in weight loss responses to exercise must be careful to control for these covariables either by matching in experimental designs or by appropriate statistical adjustments when feasible.

Age

Because the risk of chronic disease increases markedly with sedentary lifestyles and with age, the public health burden associated with inactivity is substantial among middle-aged and older adults (88). In general, lower levels of physical activity are associated with higher body weight and body fat in middle-aged and older adults (4;87;112-114). The epidemiologic studies to date provide clear longitudinal evidence linking habitual physical activity to the prevention of excess weight gain in both men and women (100-105;115) and this is true even in older age. Although the effect sizes from these observational studies appear small, over the lifespan these small savings in excess weight gain accumulate into net savings that are quite meaningful with regard to minimizing the risk of obesity-related disorders. Moreover, the longitudinal epidemiologic evidence suggests that as people progress from young adulthood to old age, they require increasing amounts of daily energy expenditure to maintain a constant body weight (37;104;105;115). More than likely, this is due to a combination of physiologic (e.g., sex hormone depletion, decline in peak aerobic capacity) and lifestyle changes (e.g., retirement) that occur with aging that make older people more susceptible to positive energy balance and thus to weight gain.

An active lifestyle also is beneficial in preventing weight **loss,** an increasingly important concern for the oldest sectors of the population (those older than 85 years) because of its relation to metabolic disorders and functional ability. Several observational studies have demonstrated the longitudinal benefits of even modest levels of physical activity on preventing excess weight loss in older age, presumably through the maintenance and preservation of lean mass (116-118).

Among intervention studies, training protocols are too variable and sample sizes are often too small to establish dose-response relations between changes in weight and activity type, duration, and intensity for different age subgroups. Nonetheless, some intervention studies have demonstrated statistically significant improvements in various weight-related outcomes (e.g., BMI, body fat distribution) with aerobic and resistance training in older participants (e.g., 8;89;108), whereas others have not (104;105). The magnitude of improvement observed in many of these intervention studies is similar, but is smaller than what is often observed in younger populations given the same relative exercise dose. A similar relative stimulus (say 75% of VO_{2peak}) will translate into a lower absolute exercise dose in older compared with younger people (due to lower levels of lean mass and aerobic capacity) and therefore, may not result in an adequate stimulus for fat loss in older people. This may be especially true for older women.

Question 5: How Do the Physical Activity Requirements for Weight Maintenance Differ Across Racial/Ethnic and Socioeconomic Groups?

Conclusions

Although some evidence suggests possible ethnic differences, the paucity of data, particularly from the stronger longitudinal cohort or randomized, controlled intervention study designs, makes it unwise to draw conclusions as to whether physical activity requirements for weight stability or reduction differ by racial/ethnic or socioeconomic groups.

Overview

Racial/ethnic disparities in obesity prevalence are robust and persistent across socioeconomic groupings (e.g., 119-121). African Americans, American Indians/Alaska Natives, Latinos and Pacific Islanders have substantially higher BMIs than do whites and Asian Americans, and a significant interaction exists between ethnicity and sex (122). For example, 54% of African American women are obese, compared with 42% of Mexican American women and 30% of white women (4). This contrasts with the similar obesity rates among men: 34% of African Americans, 32% of Mexican Americans, and 31% of whites (4).

Greater obesity implies a lesser ability to maintain weight and avoid weight gain, which may be associated with less physical activity, more physical inactivity, or both. However, racial/ethnic differences in the contribution of physical activity to weight maintenance have been systematically examined only infrequently. Therefore, in addition to the reasons to examine whether general physical activity recommendations should differ between racial/ethnic groups (See ***Part G. Section 11: Understudied Populations,*** for a detailed discussion of this topic), specifically exploring the possible need for different recommendations to promote weight maintenance also is warranted. Available evidence suggests at least 2 possible reasons for differential influences of physical activity on weight maintenance by race/ethnicity:

1. Differences in the energy cost of physical activity, such that some ethnic groups would appear to derive lesser benefits for weight maintenance at the same level of physical activity (e.g., 123).

2. Differences in the relative contribution of physical activity and excess calories (energy expenditure versus energy intake) to weight gain, such that some ethnic groups would receive less benefit than others because physical activity contributes less to the overall equation (124).

Experimental studies in exercise physiology have suggested that lower resting energy expenditures and/or activity-related energy expenditures may contribute to higher rates of obesity in Pima Indians and African Americans than in whites (123;125;126). However, recent studies have demonstrated that these physiological differences may, in fact, be explained by racial variations in body morphology (e.g., trunk versus limb length, organ size) (127-129) that would not necessarily influence the ability to maintain weight. The precise role in weight maintenance of racial/ethnic differences in resting or activity-related energy metabolism (as opposed to age or sex-related differences) in body composition is an important area for future research.

Rationale

The Energy Balance subcommittee used a search strategy to generate 236 articles from the *Physical Activity Guidelines for Americans* Scientific Database (all age group combinations except youth, with weight and BMI as the outcome of interest, excluding studies focused on weight loss). These articles were further screened to identify studies that linked physical activity to weight-related outcomes and met the following criteria: 1) targeting an ethnic minority group; **or** 2) including subgroup analyses by ethnicity, not simply treating race/ethnicity as a co-variate and adjusting for it; **and** 3) specifying the racial/ethnic minority groups included in the analyses, not aggregating in the analyses as “non-white;” **and** 4) having a sample size of 30 or more participants or at least 30 participants per study arm; **and** 5) having a “general audience” sample (i.e., not focusing on a specific subgroup such as elite athletes or postpartum women). Even very recent studies in US locations that have large ethnic minority populations, such as Baton Rouge, LA (130) and St. Louis, MO (131), did not characterize their samples by race/ethnicity. A MEDLINE search using similar parameters to those of the Scientific Database (key words: ethnic groups AND (body composition OR body weight OR obesity) AND (physical activity OR exercise OR walking) yielded 399 articles, most of which were already included in the Scientific Database. These articles were then further screened by applying the above racial/ethnic minority inclusiveness and sample size criteria, and eliminating those intervention studies in which physical activity was not the dominant intervention component (i.e., nutrition was equally strong or stronger). Reviews of relevant studies published after 1996 (132-135) and expert referral produced an additional in press publication.

Of the 24 articles identified by this systematic review, half reported on studies that were conducted outside the United States, including 9 in Asia/Pacific Islands (China, Japan, Taiwan, India, New Zealand), 2 in Africa (Nigeria, South Africa), and 1 in Central America (Mexico). Three were longitudinal cohort studies, 7 were interventions, and 14 were cross-sectional studies.

Few of the 24 studies were population-based, and thus, findings may not be representative even of subgroups with similar sociodemographic characteristics to those studied. Relatively few studies included Latinos, currently the largest minority group in the United States, and even fewer studies included American Indians, with their tremendous intra-ethnic heterogeneity from diverse tribal origins and affiliations. Most studies of Asian Americans or Pacific Islanders took place outside of the United States, introducing further complexity. International studies were included, however, because so few domestic studies included substantive racial/ethnic diversity, particularly among those with more rigorous designs. These studies may assist in clarifying any influence of some biological or cultural differences which may persist after migration to the United States, though they are likely to be less applicable with regard to differences influenced by the specific environmental or sociocultural context.

Of the 14 cross-sectional studies, which were conducted across a broad variety of racial/ethnic minority groups, including African Americans, Nigerians, South Africans, Pima Indians, Latinos, Asian Americans, Asians, and East Indians, most found an inverse association between physical activity level and weight/waist circumference/body fat percentage (29;103;113;136-146). This finding was consistent with studies in predominantly white populations (147). Among elderly Chinese, tai chi or swimming were associated with body fat distribution (lower levels in the thigh and/or abdomen), but not with total body adiposity (145). The exceptions were found in: (1) a study of 7,503 Mexican-American immigrants in Harris County, Texas, in which physical inactivity was correlated with obesity in women but not in men (103); (2) a study of 44 African American women (14% BMI less than 25, 25% to 30% Class II or III obese) in rural areas and small cities in North Carolina, in which 3-day pedometer step counts were not correlated with BMI or waist circumference (146); and (3) a study of 263 middle-aged Chinese in Hong Kong

(40% obese, 30% completely sedentary), in which low levels of physical activity were not correlated with BMI or waist circumference (144). In these instances, it is likely that BMI and/or physical activity was insufficiently variable to detect an effect.

Longitudinal studies in predominantly white populations generally demonstrate associations between increases in physical activity and decreases in the magnitude of weight gain (147). Of the 3 longitudinal studies identified in ethnic minority populations, however, only one, a 4-city convenience sample across several US regions, The Study of Women's Health Across the Nation or SWAN, replicated this association (113). SWAN study outcomes revealed associations between increases in daily routine physical activity (active transportation and less TV viewing) and exercise/sports, and less weight gain. On the other hand, increases in physical activity, compared to baseline, were not associated with smaller increases in weight, as reflected in findings of no change or decreases in waist circumference (113). The findings of the two nationally representative samples in the United States and Japan (114;148) were essentially null. He and Baker (148) found that, between 1992 and 2000, regular recreational physical activities, of any intensity, and work-related activities were not associated with less weight gain. Race (Asian or white), education, and income were not correlated with weight gain in multivariate analyses (148). However, although data were adjusted for race/ethnicity, it is not clear whether differences in the physical activity-weight gain association were analyzed by ethnicity. Lee and colleagues (114) found no baseline association between physical activity and weight, though the mean BMIs were 23.5-23.7 across activity levels. This study apparently did not examine the relationship between changes in physical activity and BMI changes. Thus, too few studies are available to draw conclusions about the influence of race/ethnicity on the association between physical activity and weight change over time.

Intervention studies selected for this review generally demonstrated that resistance training, alone or in combination with moderate- to vigorous-intensity aerobic physical activity, was necessary to produce changes in BMI or body composition/distribution in ethnic minority populations (48;67;89;149-152), despite the effectiveness of aerobic physical activity alone in improving non-weight-related aspects of the metabolic profile, such as reducing blood pressure (67;149). Wilmore and colleagues (48) presented the only within-study "head-to-head" inter-racial comparisons, with subgroup analyses after endurance training using advancing intensity and duration on cycle ergometers. The magnitude of weight loss for both whites and blacks was small; 0.2 kilogram (0.4 pound) mean weight loss in both groups. The change was statistically significant in whites but not blacks likely due to the larger sample size for whites (n=398) than blacks (n=159). Changes in various measures of body fat followed a similar pattern, with small but somewhat greater changes occurring in whites than blacks (e.g., change in sum of skinfolds for whites = -7.1 ± 0.8, blacks = -4.1 ± 1.5, $P<0.05$ for both). The ages (34.8 and 32.3 years for whites and blacks, respectively) and BMI (25.0 and 26.6 kg/m^2, respectively) were similar. Adjustments for the subtle racial/ethnic variations identified in experimental exercise physiology studies (e.g., 128) apparently were not performed (48). Wilmore and colleagues (48) concluded that the magnitude of the changes in body composition was not biologically significant in either blacks or whites and that a physical activity intervention of greater volume or longer duration was needed to produce meaningful changes in body weight and fat. In another study, in Japan, even quantities/intensities of walking sufficient to increase VO_{2max} (13,500 to 14,500 steps per day in the experimental groups versus 5,800 in the control group) did not alter BMI, although the participants in this study were normal weight or minimally overweight (24.6 to 24.7 and 25.2 kg/m^2, respectively) (149). Participants were presumably Japanese, although race/ethnicity of study samples is rarely specified in these international studies. Contrasting findings were reported in another international study. In this secondary analysis of data collected routinely on government health and social services workers in Mexico, Lara and colleagues (152) demonstrated a 0.32 kg/m^2 BMI decrease, a 1.0 kilogram (2.2 pound) weight loss, and a 1.6 centimeter (1.6 inch) decrease in waist circumference at the end of 1 year after integrating mandatory 10-minute structured group aerobic-calisthenic exercise breaks during paid work time in this group of mostly middle-aged, overweight and abdominally obese workers. Although the study had no control group, secular trends documented in Mexico at that time were similar to the United States mean increases of 1 to 2 pounds (0.45 to 0.9 kilograms) in body weight and 0.5 inches (1.27 centimeters) in waist circumference per year (113;152). The fact that the subjects of the Mexican study were not volunteer participants, but rather a sample more typical of the general population, and their overweight status, compared with the mostly normal weight Japanese sample, may account for the discrepant findings.

As noted in earlier reviews (e.g., 132-134;153) there is an extreme paucity of evidence on racial/ethnic minority groups with regard to the effects of physical activity on weight maintenance. In this review, no 2 studies examined the same ethnic-sex samples — Japanese middle-aged men, Japanese elderly adults, Japanese adults 30 to 69 years of age, Alaska Native women, African American peri-menopausal women, African American and white young and middle-aged adults, Mexican middle-aged adults — much less measures of activity duration or intensity. Consequently, broad generalizations about the influence of race/ethnicity on the physical activity requirements for weight stability or reduction are premature.

Overall Summary and Conclusions

The overall conclusions of this chapter on physical activity and energy balance can be summarized as follows:

Physical Activity, Weight Stability, and Weight Loss

Regular participation in physical activity provides benefits for weight stability, but with few data on this topic from long-term studies, the optimal amount is not known. Available data from short-term clinical trials indicate that a dose of physical activity in the range of 13 to 26 MET-hours per week results in a modest 1% to 3% weight loss, consistent with weight stability over time (7-9). Thirteen MET-hours per week is equivalent to walking at a 4 mile per hour pace for 150 minutes per week or jogging at a 6 mile per hour pace for 75 minutes per week. Aerobic physical activity done at this level would reduce upward migration of individuals from one BMI category to the next. The wide range of physical activity levels (13 to 26 MET-hours per week) needed for weight stability probably reflects individual variation in the inherent (non-structured) level of physical activity and the degree to which caloric intake is increased over time when a physical activity intervention is initiated. The magnitude of weight loss resulting from resistance exercise in this review was typically less than 1 kilogram (2.2 pounds). However, this may have been affected by the relatively short duration of the study period and the increase in fat-free mass associated with this type of intervention. Although a weight loss of 5% or more of body weight can be achieved with large volumes of physical activity, a coincident dietary intervention is typically needed to achieve this goal. The dietary intervention could include maintenance of (at pre-intervention levels) or an actual reduction in caloric intake.

Physical Activity and Weight Regain

Most of the available literature indicates that “more is better” when it comes to the amount of physical activity needed to prevent weight regain following weight loss. However, as indicated above, the literature has some considerable shortcomings regarding the appropriate research design needed to directly address this question. Studies by Ewbank and colleagues (72), Jakicic and colleagues (73) and Schoeller and colleagues (74) indicate that the volume of physical activity needed to prevent weight regain following weight loss is approximately 31 MET-hours per week or 4.4 MET-hours per day. This is equivalent to walking 54 minutes per day at 4 miles per hour or 80 minutes per day at 3 miles per hour, or jogging for 26 minutes per day at 6 miles per hour.

Physical Activity and Body Composition Parameters

Ample evidence exists for a positive dose-response relation between the volume (frequency, intensity, and duration) of endurance and/or resistance exercise, the training duration, and the amount of total and regional fat loss. Moreover, the evidence suggests that regional fat loss is greater with greater amounts of exercise-induced total weight loss and among those with the greatest levels of adiposity. In the absence of coincident caloric restriction, aerobic physical activity in the range of 13 to 26 MET-hours per week results in decreases in total and abdominal adiposity that are consistent with improved metabolic function (7-9). Thirteen MET-hours per week is equivalent to walking at a 4 mile per hour pace for 150 minutes per week or jogging at a 6 mile per hour pace for 75 minutes per week. However, when more physical activity is done (e.g., 42 MET-hours per week), decreases in intra-abdominal adipose tissue approach 3 to 4 times the level seen with this range of physical activity (93).

The Effect of Sex and Age on Physical Activity and Energy Balance

Some evidence suggests that the amount of exercise necessary to maintain a constant body weight differs between men and women and increases with age due to a variety of physiological and lifestyle factors. Moreover, even within a given sex- or age-group, weight loss responses to exercise vary substantially. Thus, it is quite difficult to make a standard daily activity recommendation that relates to optimal weight maintenance for everyone. On the other hand, the evidence base is too sparse at this time to recommend differential physical activity prescriptions based on sex or on age alone.

Physical Activity Requirements Across Race/Ethnicity and Socioeconomic Groups

Although some evidence suggests possible ethnic differences, the paucity of data, particularly from longitudinal cohort or randomized, controlled intervention study designs, makes it unwise to draw conclusions as to whether the effects of physical activity on weight maintenance or loss differ by race/ethnicity or socioeconomic groups. Some of the questions outlined in this section have yet to be fully addressed, although evidence is suggestive, for example, that socioeconomic constraints, cultural preferences, and baseline levels of sedentariness or obesity make low-intensity, social-environmental interventions feasible, sustainable, and effective in many racial/ethnic minority groups (152;154-160). However, simply conducting studies that include representative sample populations will not suffice, because there likely will be too few members of any one group to disaggregate findings by socioeconomic status, race/ethnicity, and sex, or to examine interactions between these critical sociodemographic factors.

Research Needs

This review of physical activity and energy balance identified a number of research needs in each of the topic areas covered in the chapter.

Physical Activity, Weight Stability, and Weight Loss

Studies that are appropriately designed, with sufficient statistical power, and of sufficient length are needed to specifically examine the effects of varying doses of physical activity on weight loss and weight stability across a variety of population groups, especially for those in the normal BMI range. Further examination of effects of physical activity mode, intensity, duration, and frequency on weight loss and/or weight stability also would make a valuable contribution to this area. Finally, research is needed to further examine intervention strategies that are most effective at promoting and maintaining sufficient doses of physical activity that will facilitate weight loss and/or weight stability.

Physical Activity and Weight Regain

Most available literature is observational or has relied on retrospective analysis of self-selected and self-reported levels of physical activity. Use of state-of-the art technology and complete energy balance designs are absent from the literature. Specifically, adequately powered studies of sufficient duration with randomization to different levels of physical activity after weight loss appear to be lacking. This limitation needs to be addressed to adequately explore the question of how much physical activity is needed to prevent weight regain following weight loss.

Physical Activity and Body Composition Parameters

There remains a need for more RCTs to distinguish exercise effects on total and regional fat loss from those of weight loss *per se*. In addition, the large-scale use of imaging techniques is necessary to distinguish the responsiveness of subcutaneous and visceral fat depots to endurance and/or resistance training. The ability of studies to translate imaging findings into simple anthropometric measures, such as waist or abdominal circumference, would increase the clinical and personal utility of the research. Finally, there is a need to identify and to study people who are very susceptible to weight gain in the current social environment and who thus may be most resistant to weight or fat loss with exercise.

The Effect of Sex and Age on Physical Activity and Energy Balance

Journal requirements stipulating that sex- and age-specific analyses be conducted with sufficient statistical power would help to address the dearth of information pertaining to individual and population differences in body weight response to physical activity. In addition, it would be helpful to identify and study people in the current social environment who are very susceptible to weight gain and who thus may be most resistant to weight or fat loss with exercise. Studies of how susceptibility to weight gain or resistance to weight/fat loss may vary by sex and age would contribute substantially to the obesity literature.

Physical Activity Requirements Across Race/Ethnicity and Socioeconomic Groups

Two clear mandates emerge from this research synthesis. The first is to increase attention and resources for studies that focus on diverse race/ethnicity groups and lower socioeconomic status populations, or that include sufficient numbers to permit subgroup analyses by race/ethnicity or socioeconomic status. The second is to establish standards for peer-review journals that require investigators to report race/ethnicity of samples. These standards also should require investigators to conduct subgroup analyses by race/ethnicity and/or socioeconomic status if sample sizes are sufficient, rather than simply treating these as co-variates and adjusting for them.

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Part G. Section 5: Musculoskeletal Health

Introduction

The Musculoskeletal Health Subcommittee reviewed the evidence for the role of physical activity (PA) in bone, joint, and muscle health. With respect to bone health, the review focused on osteoporosis because it is the most prevalent bone disease and because physical activity is thought to play a role in the etiology of osteoporosis. In 2002, it was estimated that 7.8 million women and 2.3 million men in the United States aged 50 years and older had osteoporosis, and another 21.8 million women and 11.8 million men were at risk of the disease because of low bone mass. By 2010, it is expected that the number of women and men with osteoporosis will increase to 9.1 and 2.8 million, respectively, and the number of women and men with low bone mass will increase to 26.0 and 14.4 million, respectively (statistics from http://www.nof.org/advocacy/prevalence/index.htm; 21 January 2008). Performing regular weight-bearing and muscle-strengthening exercises is one of the universal recommendations for the general population to reduce the risk of falls and fractures (1-3). However, more specific information on the type or volume of exercise that should be performed is lacking.

With respect to joint health, the review focused primarily on osteoarthritis (OA), particularly of the lower extremity, because of its high prevalence. It is estimated that 27 million women and men in the U.S. aged 25 years and older have OA. The incidence rates are higher in women than in men, particularly for knee OA (4). Physical activity and OA have a potentially complex association, in that a certain level of mechanical joint stress is essential for good joint health but excessive joint stress may promote the development of OA.

In contrast to bone and joint health, muscle health in not linked with a specific chronic disease. Despite this, muscle mass and function are widely recognized as important determinants of risk for such chronic diseases as osteoporosis and type 2 diabetes (5). Muscle mass and function are also recognized as important determinants of physical fitness. The review focused on physical activity as a mediator of both muscle quantity (i.e., muscle mass) and quality (i.e., muscle function).

Review of the Science

Overview of Questions Addressed

This chapter addresses 5 questions about the role of physical activity in bone, joint, and muscle health:

1. Does physical activity reduce the incidence of osteoporotic fractures?
2. Does physical activity reduce risk of osteoporosis by increasing, or slowing the decline in, bone mineral density or bone mineral content?
3. Does physical activity reduce or increase the incidence of osteoarthritis?
4. Is physical activity harmful or beneficial for adults with osteoarthritis or other rheumatic conditions?
5. Does physical activity increase or preserve muscle mass throughout the lifespan? Does physical activity improve skeletal muscle quality, defined as changes in intrinsic and extrinsic measures of force-generating capacity, such as strength or power?

For each question, the Musculoskeletal Health subcommittee considered whether such factors as sex, age, or specific characteristics of the physical activity are important determinants of the health-mediating effects. Effects of race and ethnicity could not be examined because the majority of studies reviewed either did not include volunteers from underrepresented minorities or did not conduct subgroup analyses by race/ethnicity.

Data Sources and Process Used to Answer Questions

Scientific articles related to physical activity and musculoskeletal outcomes were primarily identified by using a systematic search process that relied on the *Physical Activity Guidelines for Americans* Scientific Database (see ***Part F: Scientific Literature Search Methodology*** for a detailed description of the Database). The systematic review and subsequent article abstraction process was supplemented with previously published review or meta-analytic papers, and key or important studies identified by the Musculoskeletal Health subcommittee and consultants. Several systematic review or meta-analytic articles and faculty-identified studies were used to document the scientific evidence pertaining to physical activity and bone mineral density (BMD) and/or bone mineral content (BMC) outcomes. The systematic review and abstraction process also was used to identify articles related to physical activity and bone outcomes in men. Along with the systematic review and abstraction process, review articles, and faculty-identified key studies were used to identify papers and findings related to physical activity and joint outcomes, primarily focusing on OA. Longitudinal cohort studies and case-control studies were located that evaluated some measure of physical activity as the exposure and incidence of OA as the outcome. Randomized controlled trials (RCTs) were identified to determine the risks and benefits of physical activity among persons with OA or other rheumatic conditions, such as rheumatoid arthritis, fibromyalgia, lupus, and ankylosing spondylitis. Exercise interventions that were primarily clinical (i.e., therapeutic physical or occupational therapy) were excluded. Review articles and/or meta-analytic studies and a faculty-generated search for relevant studies were used to evaluate the evidence for physical activity and muscle fitness.

Question 1. Does Physical Activity Reduce the Incidence of Osteoporotic Fractures?

Conclusions

Physical activity is inversely associated with fracture risk (i.e., increased PA, decreased fracture risk), particularly for fractures of the proximal femur. It also has a dose-response relation with fracture risk, such that a greater volume of physical activity (i.e., frequency, duration, and/or intensity) confers greater risk reduction. It is not currently possible to identify more precisely the characteristics of the type or dose of physical activity likely to optimize fracture prevention. Based on epidemiologic studies that evaluated dose-response associations in various quantifiable manners, the minimal levels of physical activity that were significantly associated with reduced fracture risk were **at least** 9 to 14.9 metabolic equivalent (MET)-hours per week of physical activity, **more than** 4 hours per week of walking, **at least** 1,290 kilocalories per week of physical activity, and **more than** 1 hour per week of physical activity.

Rationale

No large RCTs have been conducted to determine whether the incidence of fractures is decreased in response to physical activity. Therefore, definitive evidence for its efficacy in fracture prevention is lacking. However, prospective cohort (6-16), retrospective cohort (17), case-control (18-23), a small RCT (24), and cross-sectional (25;26) studies provide moderate evidence for an inverse association of physical activity with fracture risk (i.e., high levels of activity, low fracture risk). These studies also provide evidence for a dose-dependent association with fracture risk, with higher levels of activity related to lower fracture risk. Data that can be used to develop quantifiable recommendations for the type, frequency, duration, and intensity of physical activity most likely to reduce fracture risk are limited.

The likelihood that a RCT of PA with osteoporotic fracture as a primary outcome will ever be conducted is remote because of the large sample size and long duration of intervention that would be required. In this context, the consistency of findings, from both the population studies considered in this section and the biomarker (i.e., BMD) studies considered for Question 2, provides a solid evidence base for a role of physical activity in preserving bone health. The optimal type and dose of activity necessary to maintain bone health is less clear.

The evidence will be discussed with respect to whether the associations between physical activity and fracture risk are consistent across the types of studies that have been conducted, and whether findings are influenced by such factors as sex, fracture site, or type of activity.

Type of Study

Prospective cohort studies (6-16), a retrospective cohort study (17), case-control studies (18-23), a small RCT (24), and cross-sectional (25;26) studies provide moderate evidence for an inverse association of physical activity with fracture risk (i.e., high levels of activity, low fracture risk). Overall, and without respect to the specific factors that will be considered below (i.e., type of study, fracture site, sex specificity, dose-response association), all types of observational and experimental approaches provided evidence for a role of physical activity in preventing fractures. Of the 21 studies considered, only 3 reported no associations (12;16;17), and 2 reported an association of physical activity with **increased** fracture risk under some conditions (19;20).

Prospective and Retrospective Cohort Studies

Of the 12 prospective and retrospective cohort studies, 9 found beneficial associations of physical activity with fracture risk (6-11;13-15); the others found no significant associations. Of note, 2 of the latter studies focused only on vertebral fracture risk (12;16); and the third focused on all osteoporotic fractures (i.e., hip, leg, wrist, pelvis, spine, rib, humerus, clavicle, radius, and ulna) (17). Because the effects of mechanical loading on bone metabolism are specific to the region undergoing loading, physical activity would not be expected to have uniform effects in all skeletal regions. Also, the less consistent evidence for an association of physical activity with vertebral fractures may be related to difficulties associated with diagnosis.

Case-Control Studies

Most of the case-control studies were focused on hip fracture cases (18;20-23); only 1 evaluated the role of physical activity levels as a determinant of vertebral deformity (19). Although all reported favorable odds ratios for a physical activity-related reduction in fracture risk under some conditions, 2 studies noted a direct association (i.e., increased fracture risk with increased activity) in certain cases (19;20). Silman and colleagues (19) found that heavy levels of physical activity in early and middle adult life were associated with **increased** risk for vertebral deformity in men (odds ratio [OR] 1.5 to 1.7; all $P<0.01$), but not women. The same study found that current walking and/or cycling more than 30 minutes per day was associated with a reduced risk of vertebral deformity in women (OR 0.8; 95% confidence interval [CI] 0.7-1.0), but not men (OR 0.9; 95% CI 0.8-1.2). Stevens and colleagues (20) found that vigorous activity was associated with a **reduced** risk for hip fracture in older women and men who had no limitations in activities of daily living (ADLs) (OR 0.6; 95% CI 0.4-0.8), but an **increased** risk (OR 3.2; 95% CI 1.1-9.8) in those who had 1 or more limitations in ADLs.

Randomized Controlled Trials

One small RCT reported on the incidence of vertebral fractures (24). Women who had been randomized to participate in a 2-year back strengthening exercise program or a non-exercise control group were evaluated 8 years after the completion of the intervention trial. The incidence of vertebral fractures was significantly lower in exercisers (1.6%) than in controls (4.3%).

Cross-Sectional Comparison Studies

Nordstrom and colleagues (26) compared the incidence of fractures in former elite male athletes (soccer and ice hockey players, aged 60 years and older) and age-matched male controls. The incidence of fractures before the age of 35 years was higher in the athletes than in controls (17.5% versus 12.9%, $P<0.05$), but athletes had fewer fractures than controls after the age of 50 years (8.5% versus 12.9%, $P<0.05$). Ringsberg and colleagues (25) evaluated fracture risk in older (aged 65 to 75 years) and elderly (aged 76 to 89 years) women who reported regular participation in exercise classes (at least 1 hour per week) for at least 20 years. They were compared with randomly selected age-matched women from either urban or rural communities. The relative risk for any fracture was reduced in both older (RR 0.50; 95% CI 0.33-0.79) and elderly (RR 0.28; 95% CI 0.13-0.56) regular exercisers when compared with urban controls, but not when compared with rural controls (older: RR 1.10; 95% CI 0.63-2.00; elderly: RR 0.63; 95% CI 0.24-1.43). Similar associations were found when only fragility fractures were considered.

Summary

Cohort, case-control, and cross-sectional comparison studies all provide evidence for a beneficial association of physical activity with fracture risk. A limitation of these types of studies is that they do not isolate the role of physical activity as being causal in fracture reduction. However, the general consistency of favorable findings across multiple studies generates confidence that it plays a central role, if not a causal role, in the prevention of fractures.

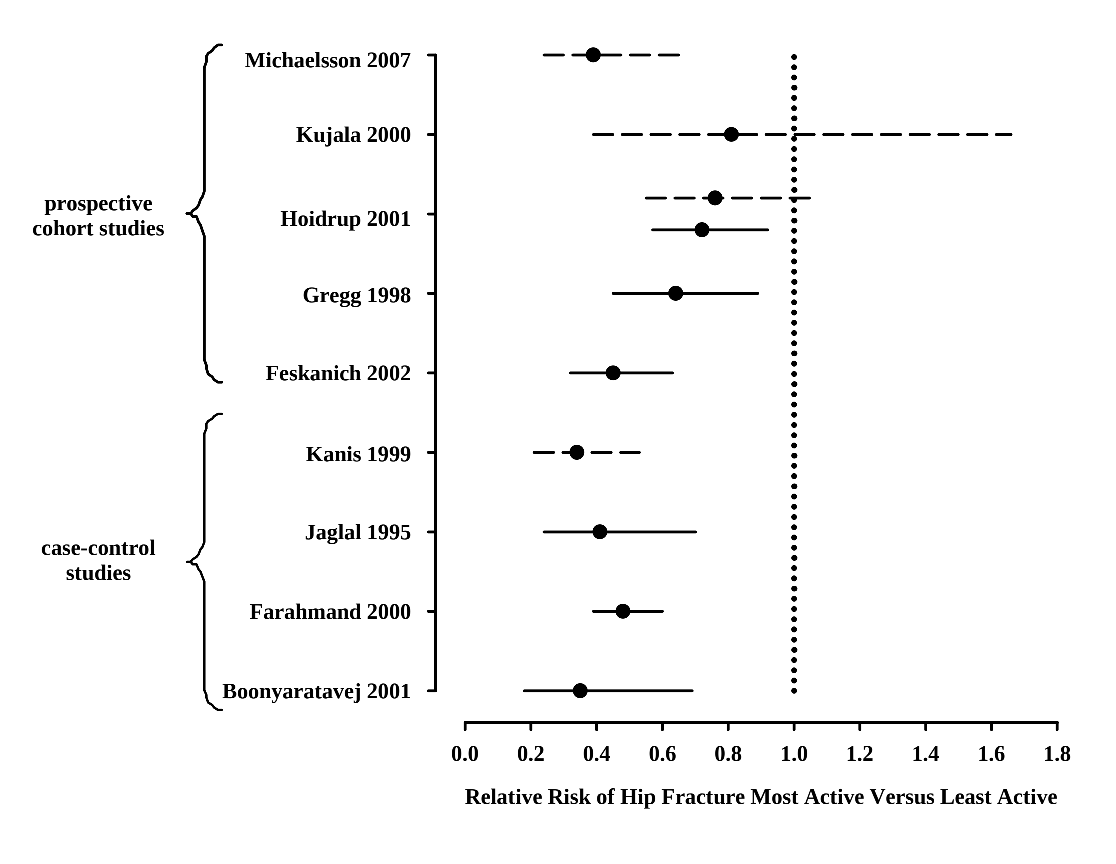
Type of Fracture

Hip Fractures

Findings show consistently favorable associations of physical activity with reduced hip fracture risk (6-9;13;18;21-23;26). Many of these studies categorized participants by levels of activity (e.g., tertile or quartile, hours per week) (6-9;13;18;21-23), and the relative risk for hip fracture was significantly reduced in the most active group when the least active group was used as the reference group (Figure G5.1).

Hip fracture risk was also increased in the least active group, when the most active group was used as the reference group: Hazards Ratio=2.56 (95% CI 1.55-4.24) (13); reciprocals of the hazards ratio and confidence intervals were calculated for inclusion in Figure G5.1. It should be noted that prospective cohort studies query for physical activity level and then monitor for fracture outcomes, whereas case-control studies query for physical activity after identifying fracture cases and controls.

Figure G5.1. Point Estimates of Relative Risk (± 95% Confidence Intervals) of Hip Fracture From Studies That Examined Multiple Levels of Physical Activity (Most Active Group Versus Least Active Group)



Note: Solid confidence intervals indicate studies of women; dashed confidence intervals indicate studies of men.

Michaelsson 2007 (13); Kujala 2000 (9); Hoidrup 2001 (8); Gregg 1998 (7); Feskanich 2002 (6); Kanis 1999 (23); Jaglal 1995 (22); Farahmand 2000 (18); Boonyaratavej 2001(21)

Figure G5.1. Data Points

Studies	Sex	Lower CI	Point Estimate	Upper CI
Prospective Cohort: Michaelsson 2007 (13)	Men	0.24	0.39	0.65
Prospective Cohort: Kujala 2000 (9)	Men	0.39	0.81	1.66
Prospective Cohort: Hoidrup 2001 (8)	Men	0.55	0.76	1.07
Prospective Cohort: Hoidrup 2001 (8)	Women	0.57	0.72	0.92
Prospective Cohort: Gregg 1998 (7)	Women	0.45	0.64	0.89
Prospective Cohort: Feskanich 2002 (6)	Women	0.32	0.45	0.63
Case-control: Kanis 1999 (23)	Men	0.21	0.34	0.53
Case-control: Jaglal 1995 (22)	Women	0.24	0.41	0.70
Case-control: Farahmand 2000 (18)	Women	0.39	0.48	0.60
Case-control: Boonyaratavej 2001 (21)	Women	0.18	0.35	0.69

Vertebral Fractures or Deformity

Although both vertebral and hip fractures are of high clinical significance because of the associated morbidity and mortality, the former are more difficult to diagnose because they can occur without symptoms. Consensus also is lacking on what extent of vertebral deformity constitutes a fracture. The few studies that have evaluated the association of physical activity with risk of vertebral fracture (or deformity) have had discordant findings (7;12;16;19;24). Heavy levels of activity in early and middle adult life were associated with **increased** risk for vertebral deformity in men (ORs 1.5 to 1.7; all $P<0.01$), but not women (19). In that study, current walking and/or cycling more than 30 minutes per day was associated with a **reduced** risk of vertebral deformity in women (OR 0.8; 95% CI 0.7-1.0), but not men (OR 0.9; 95% CI 0.8-1.2). Two other studies that assessed historical and recent occupational and leisure-time physical activity found **no associations** with vertebral fractures in women and men (12;16). However, in women aged 65 years or older, participation in moderate- or vigorous-intensity sport or recreational activity was associated with **reduced** risk for vertebral fracture (RR 0.67; 95% CI 0.49-0.94) when compared with women who reported no participation in such activities (7). In a small prospective study of women who had participated in an exercise program focused on strengthening back extensor muscles, the prevalence of vertebral fractures 8 years later was significantly lower in the exercisers than in the controls (1.6% vs. 4.3%; $P=0.029$) (24).

Wrist Fractures

Although the wrist is a common site of osteoporotic fracture, it is of lesser clinical significance than the spine and hip because the associated morbidity and mortality is very low. In the Study of Osteoporotic Fractures (7;26), physical activity was not associated with risk of wrist fracture, whereas favorable associations with risk of hip and vertebral fractures did exist. Physical activity was associated with reduced wrist fracture risk over 25.2 years of follow-up in the Adventist Health Study (high versus none/low physical activity, relative risk [RR] 0.61; 95% CI 0.41-0.87) (10), and former elite athletes were found to have a lower prevalence of wrist fractures after the age of 50 years than were age-matched controls (0.75% vs. 3.5%, $P<0.05$) (26).

All Fractures, Fragility Fractures, or Nonvertebral Fractures

Several studies have evaluated the association of physical activity with risk of any fracture (11;13;20;25), fractures in weight-bearing versus non-weight-bearing regions (15), and low-trauma, osteoporotic, or fragility fractures (14;17;25;26). The majority of these studies found an association with reduced fracture risk (11;13-15;20;25;26), but there were exceptions. Participation in vigorous levels of activity was associated with a reduced risk of fractures in women and men with no limitations in ADLs, but an increased risk in elderly with any ADL dependency (20). Joakimsen and colleagues (15) found that women and men in the highest category of physical activity, compared with those in the lowest, had a reduced risk for fractures in weight-bearing regions (RR 0.6; 95% CI 0.4-0.9) but not in non-weight-bearing regions (RR 1.0; 95% CI 0.7-1.2). Among women and men in the

Rancho Bernardo study, physical activity was not significantly associated with osteoporotic fractures (17).

Summary

The evidence supports favorable associations of physical activity with reduced risk of fractures. The evidence is most consistent for a reduction in hip fracture risk. Because the proximal femur undergoes loading during walking and all activities that involve ambulation, it is logical that an effect to reduce fracture risk would be most apparent at this site. The less consistent findings for an association with reduced vertebral or other osteoporotic fractures should not be interpreted as evidence that physical activity is not important for preventing such fractures. It is likely that the instruments commonly used to assess total physical activity do not adequately capture or characterize the potential site-specific skeletal benefits of certain types of activity.

Sex Specificity

All of the studies that included women only reported favorable associations of physical activity with reduction in fracture risk (Table G5.A1, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/) (6;7;10;18;21;22;24;25). Similarly, all of the studies that included men only reported favorable associations with reduction in fracture risk (Table G5.A1) (9;13;14;23;26).

In contrast, the studies that included both sexes had discordant findings. Three of these studies found no significant associations of physical activity with fracture risk when analyses were performed by sex (12;16;17) or in women and men combined (17). However, none of these studies was focused on hip fractures. Two studies reported an association with reduced risk for any fracture in both women and men (11;20). Other studies found beneficial associations of in women but not men (8;19), or in men but not women (15). Another noted an adverse association in men, but not women (19).

Summary

Studies that included both women and men are characterized by greater discordance in the results than those that included only women or only men. This causes a general concern regarding the assessment of physical activity in studies that include both sexes. It is typically categorized by participation in activities of varying intensity (e.g., mild = normal walking, moderate = fast walking, strenuous = jogging (17)) and, in some cases, quantified by the absolute intensity of the activity in metabolic equivalents (METs). However, these approaches do not account for sex-related differences in the **relative** intensity. In age-matched women and men, walking at a given speed or performing an activity of a certain MET level represents a greater relative cardiovascular stress for women than men, because women have a lower maximal aerobic power (27). Similarly, such activities may also represent a greater skeletal stress in women, because bone size and mineral content are less in women than in men. The failure to account for such sex-related differences in relative intensity may result in miscategorization of level of activity. For example, fast walking may, indeed, be a moderate-intensity activity for older men, but is likely to be a strenuous activity for older women. Although studies typically adjust for effects of sex (and age) in statistical analyses, it is not clear whether such approaches adequately control for these issues. The use of very broad categorizations (e.g., mild versus moderate versus strenous) may obscure true associations of physical activity with fracture risk, and this would be expected to be of greater concern in studies that included both women and men.

Physical Activity Dose-Response Pattern

Studies of laboratory animals indicate that the adaptation of bone to mechanical loading is dose-dependent, with the **intensity** of the loading force being the key determinant of the magnitude of the adaptive response (28). If these findings have relevance to human physiology, it would be expected that associations of physical activity with fracture risk would reflect a dose dependency.

Quantified Dose Response

Several studies evaluated physical activity in a manner that enabled the evaluation of a quantifiable (in terms of frequency, duration, and/or intensity) dose-response association with fracture risk. Some studies (6;7;18;23), but not others (8;9;12), found evidence of a linear trend for increased volume of physical activity and reduced fracture risk. The manner in which the dose was quantified varied among studies, including MET-hours per week, kilocalories per week, and hours per week; none of these approaches facilitated the isolation of intensity as a mediator of fracture risk. Among the studies that reported a significant dose-response association, the minimal levels found to be significantly associated with reduced fracture risk were: at least 9 to 14.9 MET-hours per week of physical activity (6), 4 or more hours per week of walking (6), 1,290 kilocalories or more per week of physical activity (7), and 1 or more hours per week of physical activity (18;23). These levels were associated with relative reductions in fracture risk of 33% to 41%. With increasing levels, the relative reduction in fracture risk was 36% to 68%. Another study (6) found a dose-response association of hours spent standing per day with reduction in fracture risk. Standing 40 or more hours per week was associated with a 34% reduction in fracture risk. One study (7) also found a significant dose-response association of physical inactivity, quantified as hours per day spent sitting, and increased fracture risk. Sitting more than 8 hours a day was associated with a 37% increase in risk of fracture.

Categorical Dose Response

A few studies that used categorical methods (e.g., tertiles of activity, inactive versus active versus very active) to evaluate dose-response associations of physical activity with fracture risk found significant trends (6;7;10), whereas others did not (9;13;15-17;19;21;22). However, even in the absence of significant linear trends, several of the latter studies found that the highest categories of activity were associated with reduced fracture risk (9;13;15;21;22); the relative reduction in risk ranged from 20% to 70%. Most of the methods used to categorize level of physical activity were based on combinations of frequency, duration, and/or intensity. Of the 3 studies that categorized physical activity by intensity (e.g., low versus moderate versus vigorous walking pace) (6;7;17), two found that higher-intensity activity was associated with reduced fracture risk (6;7).

Change in Physical Activity

In the Nurses' Health Study (6), the change in hours per week of leisure-time physical activity was evaluated over the 6-year interval before the accrual of hip fracture data. A non-significant trend (P=0.07) was apparent for women who were the least active (less than 1 hour per week) at the baseline assessment to have a decreased fracture risk if they reported becoming more active. Conversely, a significant trend (P=0.004) was seen for the most active women (4 or more hours per week) at the baseline assessment to have an increased fracture risk if they reporting a decrease in activity level. Women who decreased their activity level from 4 or more to less than 1 hour per week had more than a 2-fold increase in hip fracture risk (RR 2.08; 95% CI 1.20-3.61). Among older women and men who were performing heavy outdoor work, those who reported a decrease over a 2.5-year interval had more than a 2.5-fold increase in fracture risk relative to those who maintained their level of activity (RR 2.7; 95% CI 1.14-6.62) (11). A limitation of the study was that it could not rule out the decline in physical activity as a consequence, rather than an antecedent, of the fracture. Among women and men who participated in 3 Danish longitudinal population studies (8), the change in physical activity over 2 assessment visits was evaluated as a predictor of future fracture. Participants who had been moderately active and became sedentary had a significant increase in relative fracture risk (RR 1.53; 95% CI 1.12-2.08). However, those who moved from the sedentary to the most active group also had a significant increase in fracture risk (RR 1.73; 95% CI 1.10-2.70). A case-control study evaluated change in physical activity from the recalls of historic (ages 18 to 30 years) and recent levels (18). This approach revealed no significant associations of either increases or decreases in physical activity with fracture risk.

Summary

Studies that have used either quantitative or categorical methods of discriminating physical activity dose generally support an inverse association between the level of activity and fracture risk. However, such findings are not uniform across all studies. There may be sex-and/or site-specific benefits that are not adequately captured in the instruments used to assess physical activity. Limited evidence indicates that decreases in physical activity result in increased fracture risk over only a few years in older adults. Evidence that increasing physical activity leads to a reduction in fracture risk in older adults is lacking.

Corroborating Evidence

An advantage of studies conducted in laboratory animals is that the effects of mechanical loading (i.e., physical activity) to enhance resistance to fracture (i.e., bone strength) can be assessed in a direct and quantifiable manner. Such experiments have demonstrated that small increases in BMD and BMC (e.g., 5% to 7%) translate into very large improvements in resistance to fracture (e.g., 64% to 94%) (28). In contrast, the larger improvements in BMD and BMC in response to bisphosphonate (e.g., 14% to 15%) (29) or parathyroid hormone therapy (e.g., 9% to 13%) (30) result in only proportional improvements in resistance to fracture (e.g., 7% to 21% and 12% to 17%, respectively). If such findings in laboratory animals are relevant to human physiology, it suggests that physical activity plays a critical role in fracture prevention.

Consistency of Findings With Other Recommendations

Observational studies suggest that the minimal levels likely to reduce fracture risk are 9 or more MET-hours per week of physical activity, 4 or more hours per week of walking, and 1,290 or more kilocalories per week of physical activity. These levels are consistent with the current recommendations of the American College of Sports Medicine (ACSM) and the American Heart Association (AHA) (3;31) and in the US Dietary Guidelines (32). However, 2 studies found that relative risk of fracture was significantly reduced with more than1 hour per week of activity (18;23), suggesting that even lower amounts have benefit on bone health. As reviewed in the ACSM Position Stand on *Physical Activity and Bone Health* (33), fracture risk may be reduced both by the effects of physical activity on bone metabolism (weight-bearing endurance and resistance activities), and by its effects to reduce the risk of falling (resistance, balance, and flexibility activities). Currently, no evidence is available in humans that the benefits of physical activity on fracture reduction can be achieved through multiple short bouts versus a single longer daily bout. However, studies of animals suggests that multiple short bouts should be more effective in enhancing bone strength than a single bout (28).

Question 2. Does Physical Activity Reduce Risk of Osteoporosis by Increasing, or Slowing the Decline in, Bone Mineral Density or Bone Mineral Content?

Conclusions

Exercise training can increase, or minimize the decrease, in BMD in clinically relevant spine and hip regions. The magnitude of the effect, when compared with changes in non-exercise control groups, is approximately 1% to 2 % per year for studies up to 1 year in duration. Studies involving longer periods of exercise training (i.e., more than 1 year) are sparse, but suggest that the annual rate of BMD accrual does not persist. Importantly, studies of animals indicate that small improvements in BMD in response to mechanical loading (i.e., exercise) translate into very large increases in resistance to fracture. In contrast, increases in BMD in response to pharmacological therapy (i.e., bisphosphonates, parathyroid hormone) translate into proportional improvements in resistance to fracture.

Benefits on BMD have been found to occur in premenopausal women, postmenopausal women, and adult men; the effects of physical activity on BMD of children are addressed elsewhere in the report (See ***Part G. Section 9: Youth***). Both weight-bearing endurance and resistance types of exercise programs have been found to be effective in increasing BMD. A key determinant of effectiveness is likely whether the exercise program appropriately targets the skeletal region of interest.

Rationale

Bone mineral density is the strongest predictor of fracture risk. Accordingly, many RCTs and non-randomized clinical trials (CTs) have been conducted to evaluate changes in this biomarker of fracture risk in response to exercise training, and even more cross-sectional comparisons of BMD in sedentary versus physically active people and athletes in a variety of sports and non-athletes have been published.

Because several meta-analyses of these studies have been conducted, the primary evidence base used to address Question 2 was the meta-analytic findings (Table G5.A2, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/). It should be noted that 3 of the meta-analyses included individual subject data (34-36).

The evidence for an effect of exercise training on BMD will be summarized with respect to whether findings are specific to skeletal region (lumbar spine [LS], femoral neck [FN], other hip regions), population (i.e., premenopausal women, postmenopausal women, men), type of exercise program (i.e., endurance or impact exercise, resistance or low-impact exercise), type of study design (i.e., RCT, CT), and dose-response association.

Skeletal Region

Meta-analyses have most commonly assessed BMD of the LS and FN. Other sites include the total hip, regions of the hip other than the femoral neck, the radius, and the os calcis. Because it is fractures of the hip and spine that are of greatest clinical significance, the discussion will focus on BMD of these regions. The methods of reporting the overall treatment effect varied among studies, and included absolute (g/cm^2) and relative (%) change in BMD, annualized relative (% per year) change in BMD, and effect size. Results will be discussed regarding whether changes in the reported parameters were statistically significant and, when available, the general relative magnitude of the effect will be provided.

Lumbar Spine Bone Mineral Density

Of the 15 meta-analyses, 13 evaluated whether an exercise intervention had a significant effect on LS BMD (34;36-47) (Table G5.A2). Without regard to the population or type of exercise studied, all but 3 of the meta-analyses found that exercise intervention resulted in a significant benefit on LS BMD (36-41;43;45-47). The relative magnitude of the benefit was generally 1 to 2% per year (i.e., difference between exercise and control groups). One meta-analysis reported a much larger benefit of exercise to increase LS BMD (10.7%) (45); this will be discussed further in the population section (adult men) below.

Femoral Neck Bone Mineral Density

The second most commonly assessed skeletal region was the FN (34;35;37-40;42;47). Only 2 of these meta-analyses reported significant effects of exercise training (39;40). The relative benefits of exercise on FN BMD ranged from 0.5% per year to 1.4% per year.

Total Hip or Femur Bone Mineral Density

Regions of the proximal femur other than the femoral neck that have been studied were the total hip or what was generically described as the femur (any subregion) (38;41;42;45;46;48). Significant effects of exercise training on BMD were reported in 3 meta-analyses, with benefits of 0.4%, 2.4%, and 5.9% (45;46;48).

Summary

Meta-analytic studies generally agree that exercise training has beneficial effects on LS BMD. Although a benefit of 1 to 2 % per year may seem small, this is roughly equivalent to preventing the decrease in BMD that would typically occur over 1 to 4 years in postmenopausal women and elderly men. Less evidence exists for beneficial effects of exercise training on hip BMD. Because compliance to exercise training studies wanes as the duration of the intervention increases, the majority of studies have been 12 or fewer months in duration. The rates of increase in BMD observed in studies of less than 1 year in duration do not appear to be sustained with longer-duration exercise training (49). Studies of laboratory animals indicate that increases in bone mass continue only if the loading stimulus is progressively increased, but it is unlikely that an exercise program with a continuously increasing stimulus to bone could be carried out long-term in humans. However, in adult men and women, an important goal of physical activity is to minimize age-related declines in bone mass and strength. The extent to which decreases in BMD with aging can be attenuated through long-term exercise training is not clear. Recent evidence indicates that increases in BMD in response to a 1-year exercise training program can be maintained for up to 4 years by regular exercise (49).

Populations

Premenopausal Adult Women

Several meta-analyses have either focused exclusively on premenopausal women or conducted subgroup analyses of premenopausal women (34;37;39-41). Only one of these studies reported no significant benefits of exercise training on BMD (34). That meta-analysis was of individual subject data, and included only 3 published studies. The other meta-analyses were generally consistent with the findings summarized above for skeletal regions of interest.

Postmenopausal Women

Because the highest prevalence of osteoporosis is in postmenopausal women, it is not surprising that the majority of meta-analyses have focused on this population, either exclusively or in subgroup analyses (35;36;38-44;46-48). Only 3 of these meta-analyses found no significant benefits of exercise training on BMD (35;42;44). Of these, one excluded studies that involved any intervention other than exercise, including calcium supplementation (42), one focused only on tai chi interventions (44), and one evaluated individual subject data (35). The remaining meta-analyses involving postmenopausal women were consistent with the findings summarized above for skeletal regions.

Adult Men

Fewer RCTs and CTs of the effects of exercise training on BMD have been conducted in men than in women. The only meta-analysis of studies of men included 2 RCTs and 6 CTs; the studies evaluated BMD at any skeletal region (45). The overall effect size (ES) of 0.028 was not significant, but was equivalent to a difference in BMD of 2% between exercisers (1.6%) and controls (-0.4%). Thus, the magnitude of the overall effect was similar to what has been observed in women. Subgroup analysis for age revealed a significant ES (0.605) for men older than aged 31 years (4.2% in exercisers versus -2.5% in controls), but not for men aged 31 years or younger (ES 0.066). Subgroup analysis by skeletal region revealed significant ESs for the LS (5.8% in exercisers vs. -4.9% in controls) and the femur (4.0% in exercisers vs. -1.9% in controls).

Because only one meta-analysis of studies of men has been published, the Musculoskeletal Health subcommittee also considered RCTs of the effects of exercise training on BMD in men published after the meta-analysis (50-54). Only one of these studies reported significant exercise-induced increases in BMD (51). In that study, 24 weeks of progressive high-intensity resistance training resulted in greater gains in LS and whole-body BMD than did moderate-intensity resistance training. The ineffectiveness of exercise training to increase BMD in 3 of the other studies was likely because they were conducted at only low to moderate exercise intensities (50;53;54) and because intensity was not progressively increased (50;54). The study by McCartney and colleagues (52) involved a progressive high-intensity resistance training program, but did not result in significant increases in BMD. However, in that study, half of the 6 resistance exercises that were performed involved relatively small muscle groups (i.e., ankle dorsi- and plantarflexion, arm curls) that would not be expected to have a major influence on clinically important regions of the skeleton. Thus, the volume of exercise performed that would be predicted to have favorable skeletal effects was low.

Summary

Meta-analytic findings indicate that adult women and men can increase BMD at clinically important skeletal regions through exercise training. Two analyses that included both pre-and post-menopausal women found similar relative effects of exercise training on LS and FN BMD in both populations (39;40). The other analysis that included both pre- and postmenopausal women found similar relative effects of exercise training on LS BMD, but effects on FN BMD in postmenopausal women only (41). Although some subgroup analyses have suggested relatively greater effects of exercise on BMD in men than in women, this must be interpreted cautiously. One of the RCTs was a study of the effectiveness of resistance training (RT) to increase BMD in men following heart transplantation, and both the decreases in BMD of controls and the increases in BMD of exercisers were of relatively greater magnitude than is typically observed in healthy cohorts.

Type of Exercise Program

Some of the meta-analyses evaluated effects of the type of exercise training, either by restricting inclusion to certain types of exercise programs (34;37;38;41;43;44;47;48) or by conducting subgroup analyses (40;46). The types of exercise programs have generally been categorized as either endurance (i.e., aerobic) training (ET), with an emphasis on weight-bearing activities, or RT (i.e., weight lifting). One meta-analysis focused specifically on impact versus low-impact exercise training (40); the exercise programs were aligned with the ET (i.e., impact) and RT (i.e., low-impact) categories referred to below. In general, exercise programs can be categorized as to whether they introduce stress to the skeleton primary through joint-reaction forces (i.e., low-impact, strengthening exercises) or ground-reaction forces (i.e., impact).

Endurance Training

The meta-analyses that restricted inclusion to studies of ET have found beneficial effects only on LS (43) and hip (48) BMD. One meta-analysis included only studies of walking and found a significant effect on LS BMD, but not FN BMD (47).

Resistance Training

Four meta-analyses restricted inclusion to studies of RT (34;37;38;41). Three found a significant effect of RT on LS BMD (37;38;41); the one that did not was a meta-analysis of individual subject data (34). None of the analyses found significant effects of RT on BMD of the FN (34;37;38) or other hip regions (41).

Endurance Training versus Resistance Training

Two meta-analyses included studies that involved either ET or RT exercise programs and conducted subgroup analyses by exercise type (40;46). When considering any regional BMD measurement (LS, radius, femur regions), Kelley found a significant overall effect of RT (0.7%) but not ET (46). In contrast, Wallace and Cumming found significant effects of both ET and RT on LS and FN BMD in postmenopausal women and on LS BMD in premenopausal women (40). They found no effect of ET on FN BMD in premenopausal women and the available data were not adequate to evaluate the effect of RT on FN BMD.

Summary

Evidence indicates that both ET and RT types of exercise programs can increase BMD at both the LS and hip in adults, but this is not a consistent finding across all meta-analyses. In particular, study findings differ as to whether RT has beneficial effects on BMD of hip regions. This would be expected if RT programs did not include exercises that specifically involved the musculature in the hip region, particularly because many of the exercises that target other major muscle groups are commonly performed in the seated position (i.e., very little load on the FN and other regions of the proximal femur).

Type of Study Design

The majority of meta-analyses included studies in which the assignment to exercise and non-exercise control groups was either randomized (RCTs) or non-randomized (CTs) (35-37;39;41-45;47;48). Three included only RCTs (38;40;46) and 1 meta-analysis of individual data was generated from only CTs (34).

Randomized Controlled Trials Only

All of the meta-analyses that restricted inclusion only to RCTs found beneficial effects of exercise training on LS BMD (38;40;46); 2 also found significant effects on BMD of hip regions (39;46).

Randomized Controlled Trials versus Non-Randomized Clinical Trials

Studies that evaluated whether outcomes differed by study design had discordant findings. Wolff and colleagues (39) reported that increases in LS and FN BMD were 1.5- to 2-fold greater in CTs (1.85 % per year, 1.39 % per year) than in RCTs (0.84 % per year, 0.89 % per year). Kelley (48) found significant increases in hip BMD in CTs, but not RCTs, but in another report (43), type of study design was not a significant determinant of the increase in LS BMD. Although the meta-analysis of studies of men found that increases in BMD were larger in RCTs, this finding appeared to be influenced strongly by the study of heart transplant patients (see discussion above). Finally, Kelley and colleagues (41) reported that study quality was a determinant of the increase in hip, but not LS, BMD, with higher quality studies demonstrating a benefit. Randomization is one characteristic that contributes to high quality, but other factors include blinding and attrition.

Summary

It is not clear whether non-random assignment to exercise and non-exercise groups results in an over-inflation of the effects of exercise training on BMD. Importantly, meta-analyses that restricted inclusion to RCTs reported favorable effects.

Dose–Response Pattern

The meta-analyses provided no evidence for dose-response effects of exercise training on BMD. In some cases, when a study included two exercise groups that were distinguished by exercise intensity, the meta-analyses included only the more intensive group (40;47). Several of the meta-analyses by Kelley and colleagues evaluated characteristics of the exercise programs (e.g., duration, intensity, compliance) using regression or correlation analyses, but none of these yielded significant results (36;41;43;45;46;48). However, one of the larger RCTs (n=140) of the effects of resistance exercise training on BMD of postmenopausal women found a positive association between volume of weight lifted and the change in BMD (55).

Consistency of Findings With Other Recommendations

The findings from meta-analyses of the effects of exercise intervention on BMD and BMC did not reveal dose-response effects. However, many of the intervention trials included in the systematic reviews involved a volume of exercise that is consistent with the current recommendations of the ACSM and the AHA (3;31) and in the US Dietary Guidelines (32). The ACSM Position Stand on *Physical Activity and Bone Health* (33), which was based on narrative review and consensus opinion, suggested that adults should participate in weight-bearing endurance activities 3 to 5 days per week and resistance activities 2 to 3 days per week at a moderate to high intensity (in terms of bone-loading forces) to increase, or prevent excessive loss of, bone mass. The current review did not reveal any evidence to suggest that the recommendation is inappropriate or should be modified.

Question 3. Does Physical Activity Reduce or Increase the Incidence of Osteoarthritis?

Conclusions

In the absence of major joint injury, no evidence exists to indicate that regular moderate to vigorous physical activity in amounts that are commonly recommended for general health benefits increases the risk of developing OA. In addition, limited, weak evidence is available from observational and animal studies to suggest that low-to-moderate levels of recreational physical activity, particularly walking, may provide protection against the development of hip and knee OA.

Introduction

Osteoarthritis is a relatively common degenerative condition of the hyaline cartilage lining the joints and affects nearly 27 million US adults, manifested most commonly in the knee and hip (4). Characterized clinically by joint pain, swelling, stiffness, and weakness, OA often results in increased disability and significant negative personal effects on physical function, mental health, and quality of life. Known major risk factors for OA include genetic predisposition, older age, female sex, history of joint injury, occupational load, and excess body mass (56-60). Historically, the "wear and tear" theory of joint degeneration suggests that excess force on the joint cartilage, such as accumulates from vigorous sports and occupational and daily living activities may initiate the pathophysiological process that results in clinical OA (61). However, some level of physical activity is essential for joint health. Thus, the physical activity guidelines for Americans should include a level of movement or activity to ensure good joint health, while minimizing potential deleterious forces.

The Musculoskeletal Health subcommittee examined the scientific evidence from observational epidemiologic studies that have assessed some measure of physical activity exposure before a determination of the OA status. In selecting studies from the Scientific Database, the subcommittee used the following criteria, which were thought to be most helpful in informing the development of physical activity guidelines for Americans: 1) included case-control or longitudinal cohort study design, 2) included participants typical of the general community (not specialized subpopulations of elite athletes), and 3) assessed and/or classified exposure in relation to the usual types and amounts recommended for general health benefits (3;31). A total of 12 studies (8 longitudinal cohort, 4 case-control) were used to address the research question.

Also examined were studies of elite, high-level athletes in specific sports activities to qualitatively assess those activities that may be associated with an excess risk of incident OA. Although not representative of the general population, studies of former elite and professional level athletes provide insights that may be useful in informing physical activity guideline development. Select sports have an increased risk of incident OA by virtue of such factors as the inherent risk of joint injury, the extent of impact forces delivered to specific joints, and/or the length of time and level of play while participating in the sport. We identified 16 studies of elite athletic populations representing a variety of sports and activities.

Rationale

Data from 12 observational epidemiologic studies suggest that no clear evidence exists that regular participation in moderate- to vigorous-intensity PA, in amounts commonly recommended for general health, infer a significant risk of incident lower-extremity OA (Table G5.A3, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/). Weak evidence indicates that walking and select other low-impact activities may protect against the development of OA (Table G5.1).

Five of 8 cohort studies and 3 of 4 case-control studies reported at least 1 measure of association below 1.0. For example, in a longitudinal study, participation in cross-country skiing, walking, or swimming was associated with statistically significant protection against OA (62). Theoretically, this is aligned with laboratory animal and human research showing that exercise in moderate amounts results in beneficial changes to hyaline cartilage (greater surface area, volume, glyccosaminoglycan content), synovial fluid nutrition and distribution, and quality and strength of muscles surrounding the lower extremity joints, possibly without increasing the presence of knee cartilage defects (63-66). These changes may improve the shock absorption ability, thereby reducing forces transmitted to the joint cartilage.

Two longitudinal studies reported potential protective effects of walking on joint health. One (67) reported odds ratios of 0.96 (95% CI 0.57-1.62) and 0.78 (CI 0.49-1.24) for incident radiographic, symptomatic knee OA in adults who walked less than 6 versus more than 6 miles per week, respectively. In the other study (68), women who walked more than 5 miles per week had significantly less joint space narrowing (OR 0.38, CI 0.15-0.93) than did women who walked less than 5 miles per week (Table G5-1). A nested case-control

Table G5.1. Studies Examining the Association Between Participation in Walking and Risk of Hip/Knee Osteoarthritis

Study (Year)	Study Type	OA Definition	Walking Exposure	Measure of Association OR (95% CI)
Hart et al., 1999 (68)	Cohort	Incident radiographic: 1. Joint space narrowing 2. Osteophyte formation	Walking* No = less than 5 miles per week Yes = more than 5 miles per week	Joint Space Narrowing: No = 1.0 (referent) Yes = 0.38 (0.15 – 0.93) Osteophyte Formation: No = 1.0 (referent) Yes = 0.60 (0.22 – 1.71)
McAlindon et al., 1999 (69)	Cohort	Radiographic knee OA	Number of city blocks walked per day	None = 1.0 (referent) ≥4 = 1.2 (0.4 – 3.8)
Manninen et al., 2001 (62)	Case Control	Knee arthroplasty surgery	Regularly performed exercise for at least 2 years? Walking = Yes/No	Men: No = 1.0 (referent) Yes = 0.17 (0.02 – 1.46) Women: No = 1.0 (referent) Yes = 0.32 (0.16 – 0.65)
Manninen et al., 2002 (70)	Case Control	Knee arthroplasty surgery	Occupational Walking: Low Medium High	Low = 1.0 (referent) Medium = 1.0 (0.65 – 1.53) High = 1.06 (0.68 – 1.64)
Felson et al., 2007 (67)	Cohort	Radiographic, symptomatic knee OA	Do you walk for exercise? No <6 miles/week ≥6 miles/week	No = 1.0 (referent) <6 = 0.96 (0.57 – 1.62) >6 = 0.78 (0.49 – 1.24)

CI, confidence interval; OA, osteoarthritis; OR, odds ratio

* No details were provided on the question used to determine walking in Hart el al (68). However, another published paper from the same cohort described the walking variable as less than versus greater than 5 miles per week.

study (71) did not examine walking in isolation, but classified physical activity by the amount of joint stress. Women who participated in activities requiring low joint stress, which included walking, cycling and swimming, had a 42% (OR 0.58, CI 0.34-0.99) lower risk of hip/knee OA than did women who were inactive.

However, some select groups of persons may have a moderately elevated risk of OA due to long-term participation in high-impact activities (Table G5.2).

Table G5.2. Select Individual Sports and Recreational Activities That Have Been Associated With the Development of Osteoarthritis in at Least One Study

Sports/Activities Associated With Incident OA	Sports/Activities Not Associated With Incident OA
Ballet/Modern Dance	Cross-Country Skiing
Orienteering Running	Running
Track and Field	Swimming
Football (American) Australian Rules Football	Biking
Team Sports Basketball Soccer Ice hockey	Team sports Volleyball Baseball
Boxing	Walking
Weight Lifting	Gymnastics
Wrestling	Tennis (OA in hip/knee)
Tennis	Rock Climbing
Handball	

For example, competitive athletes who participate and train at high levels (e.g., elite, professional sports, National Teams, Olympic athletes) in sports requiring high joint impact (e.g., football, track and field, soccer) for many years have higher rates of incident knee or hip OA than do non-athletes (Table G5.A3, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/). Increased risk of OA has been reported in one or more studies for the following sports: football (Australian rules), soccer, track and field, basketball, boxing, ice hockey, orienteering running, wrestling, tennis, ballet, and handball (see ***Part G. Section 10: Adverse Events f***or a discussion of muskuloskeletal injuries related to these sports). The increased risk of OA in athletes in these sports may be attributed, in part, to joint injuries, because these sports are also associated with the highest rates of joint injuries (72;73), which is a strong risk factor for incident OA (57-59). In addition, persons who have occupations that require excessive knee bending, kneeling, or twisting/torsion movements or involve high-load weight bearing (lifting and carrying heavy loads) and who also participate in moderate or vigorous recreational activity may have increased risk for lower-extremity OA due to the additive effects over time (69;74).

Special Considerations

Sex

Women have a higher prevalence and incidence of most types of OA (57;75). Women also have lower quadriceps muscle strength, one of the main muscles supporting the hip and knee

(76;77), different anatomical and biomechanical structure (78;79), higher rates of obesity (80), and participate in different types of physical activity than do men (81), and have different risks of injury even in similar sports (72;73). All these factors can influence the risk of OA related to physical activity, suggesting that the relationship may be sex-dependent. For example, quadriceps muscle strength has been shown to be an independent risk factor for the development of hip and knee OA even after controlling for excess body weight, age, activity level, injury status, and physical fitness (76). In fact, the weak protective effect of physical activity participation seems to be stronger among women than men (62;68;70;71;82). Both Rogers and colleagues (71) and Manninen and colleagues (62) reported that low and high levels of accumulated physical activity were protective for OA among women (not all were statistically significant due to small sample sizes), but only high levels were protective among men. A later study by Manninen and colleagues (70) also reported a protective effect on severe knee OA among men and women combined. Because that study was a matched (age and sex) case-control design, the independent effect of sex could not be estimated.

Excess Body Mass

It has been demonstrated that overweight and obese individuals put more stress on their lower-extremity joints during normal ambulation than do normal-weight individuals. This suggests that overweight and obesity would exaggerate impact forces transmitted to the joint during exercise and recreational physical activity, potentially increasing the risk of developing OA. However, evidence suggests that elevated body mass index (BMI) independently predicts incident OA, and that physical activity does not contribute significantly to this increased risk (67). Physical activity plays an integral role in both weight loss and the maintenance of normal body weight. Currently, no evidence supports the possibility that promoting activity in the general US population, even among those who are overweight or obese, will increase risk for OA.

Previous Injury

Previous joint injury is a well-established, independent risk factor for OA. In fact, athletes who sustain major joint injuries, such as anterior cruciate ligament ruptures, and undergo surgical reconstruction have premature onset OA (about 10 years early) compared with non-injured athletes (83-86). Athletes in some sports that involve relatively high joint impact (e.g., soccer) and who do not suffer a major joint injury do not seem to have excessive rates of incident OA (87). However, in other sports (e.g., Australian Rules Football), both players with and without previous knee injuries had an increased risk of radiographic knee OA (84).

Not all studies included in Table G5.A3 controlled for previous injury. (This table can be accessed at http://www.health.gov/paguidelines/report/). Three studies that reported an increased risk of OA associated with the highest level of physical activity (74;82;88) did not control for previous joint injury, which may explain some of the excess risk. Sutton and colleagues (89) reported an increased risk of knee OA with regular long walks (at least 2 miles at least 1 time per week), but this association was no longer significant after controlling for previous knee injury. McAlindon and colleagues (69) reported a significant effect of more than 3 hours per day of heavy physical activity (combined occupational, recreational, household and transportation domains) on symptomatic knee OA incidence, even after controlling for previous joint injury, BMI, age, sex, and other potential confounders. This finding is difficult to place into context in today's society. Because of changing job demands and increased technological advances in high-risk occupations (e.g., manufacturing, farming), it is likely that only a small fraction of the current US population accumulates more than 3 hours of heavy physical activity per day.

Study Design Issues

It is interesting that the few studies that reported significant protective effects of physical activity on OA incidence were case-control study designs (one was a nested case-control within a longitudinal cohort). Case-control studies are strong and efficient study designs when an outcome is rare. However, OA is a common condition when compared with the incidence of some types of cancer or even diabetes. Therefore, some biases inherent to case-control studies (e.g., recall bias, lack of representative controls) (90) may have influenced the findings. This issue remains unclear, because 2 prospective cohort studies (67;91) also reported measures of association that were below the referent level, although not statistically significant, suggesting a possible protective effect for some groups.

Last, observational study designs such as these cannot determine cause and effect. However, conducting an RCT to investigate the influence of different exercise participation on the rates of incident OA is not feasible due to the long incubation period for OA development and the potential ethical problems of randomizing persons to inactivity.

Some of the inconsistent findings also may be related to the methods used to collect and analyze self-reported data. Historically, instruments used to query physical activity behavior were designed to study the relation between activity and cardiovascular or mortality outcomes. Hence, many instruments are geared more toward how physical activity may affect the cardiorespiratory system versus the effects it may have on the musculoskeletal system. As a result, the bone and joint loading effects of physical activity may be missed in these studies. For example, jogging and swimming may be rated at the same MET level based on their cardiovascular effects, yet these two activities are very different in terms of loading delivered to the muscles, bones and joints. Hootman and colleagues (91) attempted to address this issue in part by applying a "joint loading stress score" to the self-reported data. However, the effects of joint loading physical activity on incident hip and knee OA were still difficult to identify, even in this relatively large longitudinal study. Future research should focus on teasing out the musculoskeletal effects from the cardiovascular effects in an attempt to identify the types of activities involving high joint loading that may be associated with increased risk of OA.

Another study design issue is the inconsistent definition of incident OA. Various outcomes were used across studies including self-reported doctor-diagnosed OA, radiographically-determined OA (with and without symptoms), and incident hospitalization for joint replacement surgery. It is not known how these different definitions may affect the measures of association.

Consistency of Findings With Other Recommendations

Our findings are not fully consistent with the results of a systematic review of sporting activities on the development of hip OA (92) or the OASIS group (93), but do align with the American Gerontological Society Consensus Guidelines for practice (94).

Lievense and colleagues (92) reported that moderate evidence exists that participation in a combination of team sport and running activities is positively associated with the development of hip OA. In addition, they reported conflicting evidence for ballet and soccer participation and limited evidence for general athletics. This systematic review included some of the studies reported in Table G5.A3, but also included studies published before 1995, the beginning point of this evidence synthesis (Table G5.A3 can be accessed at http://www.health.gov/paguidelines/report/). Studies completed before the early 1990s may have included subjects who were inherently different from more contemporary cohorts. Also, Lievense and colleagues (92) noted that 4 of the older studies scored very low in terms of study quality (less than 40 on a 100 point scale), which may have contributed to the disparate findings.

The OASIS group (93) stated that considerable scientific evidence indicates that sport is a risk factor for OA of the knee and hip, and that the risk correlates with frequency, duration, and level of play. This is consistent with the evidence presented in Table G5.A3. However, the OASIS group did not specifically address participation in general, moderate-intensity physical activity. The OASIS summary recommendations also stated that joint injury and excess body mass are much stronger risk factors for OA than sports participation. They further recommended that the high-level athlete should be informed of the risk of OA associated with sports and counseled regarding protecting joints from trauma and maintaining optimal body weight. This guidance is an important risk communication message for any person engaging in high-level sports activity over many years.

Summary

In the absence of joint injury, participation in recreational or leisure physical activities at levels commonly recommended for general health benefits does not increase the risk of developing OA. However, long-term high-level participation in select high-impact sports (e.g., football, soccer, track and field) may be associated with increased risk of OA. As such, health promotion messages should be developed to inform persons choosing to participate in such activities that they may have increased risk for OA, and that modifying other OA risk factors (e.g., maintaining normal body weight, preventing joint injuries) may help to lower risk.

Question 4. Is Physical Activity Harmful or Beneficial for Adults With Osteoarthritis or Other Rheumatic Conditions?

Conclusions

Strong evidence indicates that both endurance and resistance types of exercise provides considerable disease-specific benefits for persons with OA and other rheumatic conditions without exacerbating symptoms or worsening disease progression. Adults with OA can expect significant improvements in pain, physical function, quality of life and mental health and delayed onset of disability by engaging in appropriate low-impact physical activity for approximately 150 minutes per week (3 to 5 times per week for 30 to 60 minutes per session). No evidence indicates that OA is a contraindication for participation in physical activity among sedentary populations. However, patients should be counseled to pursue activities that are low impact, not painful, and do not have a high risk of joint injury.

Introduction

More than 46 million adults in the United States have arthritis or another rheumatic conditions and almost 40% of them are limited in their usual activities by their condition (95). As a result of the aging of the population, the prevalence of arthritis is expected to grow to 67 million by the year 2030 (96), and more than 44% of adults with arthritis are sedentary (97). Because adults with arthritis make up a significant proportion (21%) of the general US population (95) and have disease-specific barriers (e.g., pain, fatigue) to initiating and maintaining physical activity (98-100), Federal authorities should consider this patient population in the physical activity guideline development process.

To evaluate the evidence regarding the disease-specific benefits of PA among adults with arthritis, the Musculoskeletal Health subcommittee examined RCTs published since 1995 (Table G5.A4, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/). These studies met the following criteria: 1) included only patients with arthritis or another rheumatic condition (e.g., OA, rheumatoid arthritis, fibromyalgia, lupus, gout), 2) compared an exercise group (i.e., endurance and/or resistance exercise) with a non-exercise control group, 3) reported adequate information on the intervention (e.g., type, frequency, duration), and 4) reported patient-oriented outcomes such as pain, physical function, quality of life, and disability. Studies that described a clinically-delivered exercise intervention (e.g., therapeutic physical or occupational therapy) were excluded.

Rationale

Table G5.A4 includes findings of 24 exercise intervention studies (15 endurance, 9 resistance, and 5 combined endurance plus resistance training) (Table G5.A4 can be accessed at http://www.health.gov/paguidelines/report/). Interventions were included if the exercise program described could feasibly be replicated in community settings (e.g., group exercise classes, home programs) even if they were supervised by health care or research professionals such as a nurse, physical therapist, or exercise physiologist. The 15 endurance exercise studies represented 17 actual exercise versus non-exercise control comparisons, because 2 studies (101;102) had multiple endurance exercise groups. Both endurance and resistance exercise training programs demonstrated effectiveness for reduced pain, improved function, and additional benefits on quality of life, mental health, self-efficacy (confidence), and delayed onset of disability in ADLs.

Components of the Exercise Prescription

Table G5.3 summarizes characteristics of the exercise RCTs among those with arthritis or other rheumatic conditions.

Many studies did not measure the *actual* dose of exercise delivered during the course of the intervention, but *prescribed* doses of exercise across all 24 studies averaged 146 minutes per week of moderate-intensity exercise, such as walking, cycling, tai chi, and water aerobics. Average frequency (2.8 days per week) and duration of exercise sessions (51.8 minutes per day) were consistent with current recommendations for people with arthritis (2003), and with recommendations for the general adult population in the United States (3;31). The length of the interventions varied considerably, ranging from 8 to 104 weeks.

Endurance Exercise Versus Control

The 15 endurance exercise studies (17 comparisons) included participants with OA (n=12), fibromyalgia (n=4) and rheumatoid arthritis (n=1). The modes of exercise, all moderate intensity, included walking (n=5), tai chi (n=5), water exercise (n=2), aerobics class (n=2), and cycling (n=1). Participants exercised in small groups or at home for an average of 2.9 times per week and 48 minutes per session for a total average of 137 minutes per week. Endurance interventions lasted an average of 23.9 weeks (range, 8 to 72 weeks). Sample sizes were variable, with an average of 50 subjects in the exercise arm and 45 in the control arm. Only 1 trial, the Fitness Arthritis and Seniors Trial (3 separate reports (103-105), had more than 100 subjects in both the exercise and control arms.

Pain reduction and improvements in physical function were reported in the majority of studies of endurance exercise. Other benefits included improved self-efficacy (confidence), quality of life, muscle strength, mental/emotional health, and physical activity levels. No increases in symptoms (pain, fatigue, stiffness) or other measures of disease activity (e.g., global rating, radiographic progression, inflammatory markers) were demonstrated. In fact, Schachter and colleagues (102) reported decreased disease severity (physician global rating of severity and Fibromyalgia Impact Questionnaire total score) in response to exercise training for subjects who adhered to both long-bout (one 30-minute bout per day) and short-bout (two 15-minute bouts per day) programs.

Table G5.3. Summary Descriptive Characteristics of the Randomized Controlled Trials of Exercise Among Persons With Arthritis or Other Rheumatic Conditions

Study Type	Number of Studies	Average (Mean) Characteristics of Interventions Number of Intervention Subjects [Range]	Average (Mean) Characteristics of Interventions Number of Control Subjects [Range]	Average (Mean) Characteristics of Interventions Length (Weeks) of Intervention [Range]	Average (Mean) Characteristics of Interventions Frequency Per Week [Range]	Average (Mean) Characteristics of Interventions Duration (Min) Per Session [Range]	Average (Mean) Characteristics of Interventions Total Prescribed Dose (Min/Week) [Range]	Significant Findings (Number of Studies/Outcome)
Endurance versus Control	17†	50 [17–144]	45 [16–149]	23.9 [8–72]	2.9 [2–5]	47.8 [20–60]	137 [60–180]	10 ↓pain 8 ↑ function 1 ↑ quality of life 4 ↑ self-efficacy 4 ↑ muscle strength 2 ↑ physical activity 3 ↓ symptoms (other than pain) 4 ↑ mental/emotional health 5 ↑ or no change in symptoms/ disease activity
Resistance versus Control	9	54 [10–146]	55 [10–149]	50.9 [8–96]	2.6 [2–3]	52.5 [30–60]	145 [60–180]	5 ↓ pain 5 ↑ function 6 ↑ muscle strength 3 ↓ stiffness 3 ↓ disease activity 4 ↓ disability 1 ↑ ROM
Combination versus Control	5	62 [25–151]	64 [25–158]	44.0 [12–104]	3.0 [2–5]	55.0 [30–75]	156 [120–180]	1 ↓ pain 2 ↑ function 2 ↑ muscle strength 2 ↑ fitness/perceived exertion 2 ↑ no change in disease activity 1 ↑ mental health 1 ↓ body weight
All Studies	24‡	54	52	39.6	2.8	51.8	146	–

* All studies implemented exercise interventions of at least moderate intensity.

†The endurance group had 15 individual studies, but 17 actual exercise versus control comparisons.

‡ Review included 24 individual studies, 2 studies compared multiple exercise groups versus a non-exercise control group and may be counted separately under the rows for the endurance, resistance, and combination studies.

Resistance Exercise Versus Control

The 9 resistance exercise studies included patients with OA (n= 5), rheumatoid arthritis (n=3), and fibromyalgia (n=1) who exercised in groups at a clinic or other exercise facility (n=7) or at home (n=2). Seven studies used isotonic (i.e., dynamic resistance exercise involving concentric and eccentric actions) and 2 used isokinetic (i.e., variable resistance, constant velocity) resistance training modes. Exercise occurred an average of 2.6 times per week for 52.5 minutes per session, accumulating an average of 145 minutes per week. The duration of resistance interventions ranged from 8 to 96 weeks (average 50.9 weeks). The average number of subjects in the exercise arms was 54 versus 55 in the control arms. Only one trial, the Fitness Arthritis and Seniors Trial (3 separate reports (103-105) had more than 100 subjects in both the intervention and control groups.

Benefits of resistance exercise for adults with arthritis included improvements in muscle strength, symptoms (pain and stiffness), and function. Reduced risk of incident disability in ADLs and improved measures of disease activity also were noted. Using two common measures of disease activity (Disease Activity Score 28 [DAS28], which captures joint tenderness, patient global rating of health, pain visual analog scale and erythrocyte sedimentation rate, and the Larsen Score, which measures radiographic damage), 2 studies of patients with RA reported significant improvements in DAS28 scores in response to resistance training (106;107) and no worsening of the Larsen Score (106).

Combined Interventions Versus Control

The 5 studies that examined a combined endurance and resistance intervention included patients with OA (n=4) and RA/inflammatory arthritis (n=2) patients. The mode of endurance exercise was walking in 3 studies and cycling in 2 studies. The mode of resistance exercise was either isotonic (n=3) or isokinetic (n=1). One study did not report mode. Combined interventions occurred on average 3 days per week and averaged 55 minutes per session, for a total average weekly dose of 156 minutes per week. The average duration of the combined interventions was 44 weeks (range 12 to 104 weeks). The average number of subjects in the combined exercise arm was 62 versus 64 in the control arm. Munneke and colleagues (108) and de Jong and colleagues (109) were the only studies that had more than 100 subjects in each group.

Benefits of intervention programs that included both endurance and resistance exercise have been similar to those reported for endurance-only and resistance-only interventions. The benefits include reduced pain and improved function, muscle strength, fitness, and mental health, with no increase in disease activity or symptoms. Weight loss and improved satisfaction with function also were reported benefits. Specifically, the Arthritis, Diet, and Activity Promotion Trial (ADAPT) (110) noted that the endurance plus resistance exercise arm reduced body weight by 2.6% compared to 1.3% in the education control arm.

Special Considerations

Appropriate Physical Activity Type and Dose

The exercise prescriptions in the reviewed studies varied widely on the frequency, duration, intensity and type of physical activity. Thus, it is difficult to define either a minimum dose of activity that results in clinical benefits for adults with arthritis or a maximum dose that may be associated with increased symptoms or adverse events. The average minutes per week of activity prescribed in these studies (146 minutes per week) suggests that a prescription of 5 days per week for 30 minutes per session is likely appropriate for most people with arthritis. All reviewed studies prescribed moderate to vigorous intensity and low-impact activities. However, it is unclear whether some persons with arthritis can tolerate higher-impact activities, such as team sports or tennis. It seems appropriate, given the evidence, to guide persons with arthritis toward low-impact, moderate-intensity activities, such as walking, cycling, water exercise, and tai chi.

In fact, walking may be a particularly relevant exercise mode for persons with arthritis, especially in terms of disability prevention and safety. Walking was the exercise mode of choice for 9 studies (6 endurance and 3 combined), and those studies reported benefits in terms of reduced pain and improved function among persons with rheumatic conditions. No true dose-response studies have been conducted, but evidence does suggest that higher compliance to endurance and/or resistance exercise was associated with better outcomes, including less disability and pain and improved physical function. Ettinger and colleagues (103) used walking as the primary endurance component of the intervention and reported on global ADL disability, an important patient-oriented outcome measure. The walking group reported a significant 10% lower ADL disability score and the resistance training group an 8% lower score compared to the control group. A follow-up of this study cohort (105) found that endurance exercise resulted in a 37% reduced risk of incident ADL disability and that resistance exercise resulted in a 40% reduced risk. These studies are important to highlight because of several critical design elements that are central to high study quality (111): 1) large number of subjects (endurance = 144, resistance = 146, control = 149), 2) use of an appropriate randomization protocol, 3) concealment of allocation to randomized groups, 4) low loss-to-follow-up (83% completed study), 5) adequate adherence to the assigned intervention (approximately 69%), and 6) use of an intent-to-treat analysis. In addition, Ettinger and colleagues (103) reported adverse events related to the intervention, including 2 in the endurance exercise group, 3 in the resistance exercise group, and 1 in the control group; only 2 of the 6 reported events resulted in injuries (1 in the endurance group, 1 in the resistance group).

Important Outcome Measures

Pain

A recent expert consensus document from the international group, Osteoarthritis Research International (OARSI), reported 25 evidence-based, patient-focused, recommendations for the management of knee and hip OA. (112) One of the 11 non-pharmaceutical OARSI recommendations states that all patients with hip and/or knee osteoarthritis should be counseled to engage in aerobic, resistance/strengthening, and range-of-motion exercises. This recommendation was supported by the highest level of evidence rating (1a — based on meta-analyses of RCTs) and had a 'strength of recommendation' rating of 96 (using a 0 - 100 visual analog scale). OARSI reported the effect of exercise on pain relief as moderate, as pooled effect sizes reported were 0.52 (95% CI 0.34-0.70) for aerobic exercise and 0.32 (95% CI 0.23-0.42) for resistance exercise.

Physical Activity Level

Even though the prescribed doses of physical activity in the studies included in Table G5.3 approached 150 minutes per week, a dose consistent with current recommendations, only 2 studies measured actual levels during the intervention (113;114). Both studies suggested that the interventions did, indeed, increase actual activity levels. However, without monitoring the actual participation, it is difficult to determine whether the intervention was ineffective or whether a lack of effect was related to an insufficient increase in activity. Persons with arthritis are known to have disease-specific barriers, particularly joint pain, to being physically active (98-100). If an exercise intervention protocol does not adequately address pain fluctuation during exercise, then persons with joint pain and stiffness may drop out at high rates, have lower compliance to the prescribed dose, or not respond to the intervention protocol as expected.

Quality of Life

Thirteen studies measured quality of life outcomes using various instruments, and 9 of those reported benefits, mostly in terms of the function component of quality of life. Quality of life, a concept that includes physical, mental, and emotional elements, is particularly important for people with arthritis. Arthritis is not typically associated with excess mortality, as are cardiovascular and other chronic diseases. However, it is associated with pain, functional limitation, work disability, and loss of participation in valued life activities, which severely affect quality of life. These results suggest that adequately measuring quality of life as a primary outcome measure in arthritis interventions should be a priority.

Disability

Only 2 of 24 studies (103;105) included a measure of disability, as defined by the authors. In terms of self-reported disability outcomes, the OARSI recommendations report pooled effect sizes for self-reported disability of 0.46 (95% CI 0.25-0.67) for aerobic exercise and 0.32 (95% CI 0.23-0.41) for resistance exercise (112). The International Classification of Functioning and Disability model purports participation restriction as an important concept to capture in health studies. Participation restriction goes beyond limitation in specific activities (e.g., climbing a flight of stairs, rising from a chair) by placing the activity limitation in the context of a social role (115). For example, not being able to play the piano (activity limitation) would be a significant disability (participation restriction) for a concert pianist (social role), but not for someone who does not play the piano. Therefore, it is equally important to include reliable and valid measures of function/activity limitation (self-report or performance-based), as well as measures of participation restriction in studies of arthritis treatment interventions. Participation restriction was not an outcome measure in any of the reviewed studies.

Adverse Events

Few studies reported adverse events, even though the CONSORT guidelines state it is important to report even minor adverse events from RCTs (111). However, at least 14 studies reported that arthritis symptoms (pain and/or stiffness) were improved, or at least not worsened, with exercise and at least 4 studies reported improvement or no increase in disease activity. Of the 2 studies that did report intervention-related adverse events, Ettinger and colleagues (103) reported that only 2 of 6 events resulted in injury, 1 each in the endurance and resistance exercise groups, and Coleman and colleagues (116) reported no major musculoskeletal adverse events. In addition, Fransen and colleagues (101) reported that 4 participants dropped out of the study, 2 due to aggravation of knee pain (both in the tai chi group) and 2 due to low back pain (1 each in the tai chi and hydrotherapy groups). These reviewed studies, as well as others (117), noted that the frequency of study-related adverse events were low among arthritis patients and older adults in general. This suggests that the promotion of moderate physical activity, such as walking, cycling, and water exercise, is likely safe in patients with arthritis. However, risk communication messages geared for this population should include concepts such as “start low and go slow.”

Consistency of Findings with Other Recommendations

The above recommendations agree with the OARSI expert consensus guidelines (112), the OASIS statement (93), the American Geriatrics Association Consensus Practice Statement (94), and the MOVE Consensus (118). All 4 of these consensus documents recommended that adults with OA participate in moderate-intensity, low-impact exercises with low risk of injury. Both endurance and resistance exercises are recommended, accumulating approximately 150 minutes per weeks, delivered either in group or home settings, 3 to 5 times per week for 30 to 60 minutes per session. The recommendations also are aligned with disease management guidelines of the American College of Rheumatology and the European League Against Rheumatism (EULAR) (119-121). At least 9 systematic reviews provide additional support to the recommendations in the current report (122-130).

Summary

Current scientific evidence indicates that physical activity has important health benefits for adults with arthritis, including reduced pain, improved function, and a reduced risk of disability. Such benefits have been observed in adults with arthritis who participate in moderate-intensity, low-impact activities (e.g., walking, cycling, water exercise), 3 to 5 times per week for 30 to 60 minutes per session (i.e., accumulate approximately 150 minutes per week). Both endurance and resistance exercise, performed in group or home settings, has been found to be effective.

Question 5. Does Physical Activity Increase or Preserve Muscle Mass Throughout the Lifespan? Does Physical Activity Improve Skeletal Muscle Quality, Defined as Changes in Intrinsic and Extrinsic Measures of Force-Generating Capacity, Such as Strength or Power?

Conclusions

Specific modes and intensities of physical activity can preserve or increase skeletal muscle mass, strength, power, and intrinsic neuromuscular activation. Such effects appears to be similar in women and men and pervasive throughout the lifespan, although some evidence indicates that the magnitude of the increases in skeletal muscle mass with resistance training may be attenuated in advanced age. Specific types of activity can effectively increase fat-free mass (i.e., lean mass), strength, and power. Specifically, performance of regular (i.e., 2 to 4 times per week), high-intensity (i.e., 60% to 80% of the 1 repetition maximum [1RM]), progressive resistance exercise can result in significant increases in muscle size, strength, and neuromuscular function. Endurance activities have not been shown to increase muscle mass or quality, but may be associated with an attenuation of loss. Muscle power output may be a critical determinant of physical functioning in the elderly, and evidence is emerging that resistance training performed at high velocity and low external resistance to maximize muscle power output may have important beneficial effects on physical function in older adults.

Introduction

Evidence indicates that the preservation of fat-free mass and, in particular, skeletal muscle mass is associated with favorable health outcomes with advancing age. Cross-sectional studies have reported that sarcopenia, the age-associated loss of muscle mass, is associated with muscle weakness, functional limitations, and disability (131;132). Emerging evidence for the effects of increasing adiposity on disability risk also have raised questions regarding the relative importance of sarcopenia on age-associated disability (133-135). Despite these observations, evidence remains for an important role of fat-free mass in maintaining physical functioning and preventing disability with advancing age (131;136;137). Physical activity and exercise interventions that have the potential to increase or preserve skeletal muscle mass also may have important therapeutic benefits on improving physical functioning and preventing disability, particularly in older adults (see ***Part G. Section 6: Functional Health f***or a detailed discussion of this issue). Muscle mass also has been reported to be a significant reserve of energy and a critical tissue for metabolic homeostasis during stress and chronic disease. Thus, physical activity interventions designed to increase or preserve muscle mass may be important for several health outcomes across the lifespan (5).

The effects of physical activity on muscle mass may mediate observed changes in muscle strength and, as such, are important to men and women of all ages. For example, exercise-induced increases in muscle strength are associated with improved muscular fitness in formerly sedentary obese individuals (138;139). This is particularly noteworthy because sedentary overweight and obese individuals have a limited exercise capacity (140), which may impair physical function. In older individuals, the age-related loss of muscle mass is accompanied by losses in voluntary muscle strength (141). Consequently, in those at risk of sarcopenia, functional capacity and mobility are likely to be comprised. Studies conducted in older adults indicate that increases in lower body strength are associated with improvements in gait parameters (142;143), functional capacity (144-147), and bone health (51;148;149). Strength adaptations also have been suggested to mediate increased endurance (150).

Given the current scope of physical inactivity in the United States and the declines in muscle quality parameters that begin in early adulthood, interventions designed to prevent declines in muscle quantity and quality through physical activity should be focused on all ages of the population. However, because the percentage of older Americans is increasing rapidly and the associated detriments in function may similarly escalate, a special emphasis on the importance of musculoskeletal health should be placed in this population to prevent the substantial economic costs associated with decreased physical functioning that result from the loss of muscle mass and muscle weakness.

Rationale

Physical Activity and Muscle Mass

Many studies have examined the role of physical activity on changes in body composition. Because of the association between muscle strength, power, and muscle mass and the well described age-related declines in skeletal muscle mass, we examined the literature on the influence of exercise training interventions, in particular resistance training interventions, on changes in muscle and fat-free mass. Studies that were evaluated included trials conducted in young, middle-aged, and older men and women. Very few studies, if any, examined subgroups of different ethnic populations to evaluate variations in responsiveness.

The effects of progressive resistance training in young healthy men and women have been well described (151). As reviewed by Kraemer and colleagues, high-intensity progressive resistance training in young adults results in significant increases in dynamic strength, explosive power, and muscle mass. More recent studies have confirmed these findings. Short-term studies of both lower- and upper-extremity resistance training have demonstrated increases in muscle cross-sectional area (CSA) in men (152-154) and women (155), with corresponding increases in muscle strength.

Sex-specific changes in muscle mass or CSA in response to resistance exercise training have been investigated. Short-term studies of progressive resistance training noted similar increases in muscle adaptations of men and women (156). Increases in muscle CSA by computed tomography (CT) have also been shown to be similar in men (17.5%) and women (20.4%) in response to 16 week of upper- and lower-extremity high-intensity resistance training (157). However, one study employing elastic bands for resistance training noted significant increases in muscle fiber CSAs in men, but not women, in response to 8 week of training, with 2 - 3 sessions per week (158). Interestingly, one RCT of adolescent girls demonstrated that a 5 day per week mixed mode endurance training program (running, aerobic dance, competitive sports) induced a significant (4%) increase in mid-thigh muscle volume (159). More recently, assessment of fat-free mass by dual-energy x-ray absorptiometry (DXA) and serial CT scans to measure muscle volume confirmed that similar increases in muscle mass and volume occurred in young men and women in response to a 6-month whole-body program of progressive resistance exercise training (160). These results suggest that resistance exercise training can increase muscle strength and mass to similar relative extent in men and women. Other modes of physical activity may increase fat-free mass during adolescence.

Several studies have assessed combinations of the number of repetitions and intensity of resistance training required to maximize gains in muscle strength and mass in young adults. Campos and colleagues compared the responses to 8 weeks of 3 different regimens of progressive resistance training (161). Young healthy men were randomized to perform low-repetition/high-intensity, intermediate-repetition/moderate-intensity, or high-repetition/low-intensity progressive resistance training of the lower extremities (leg press, squat, and knee extension). Increases in muscle fiber hypertrophy and muscle strength were greater in the low-repetition/high-intensity and intermediate-repetition/moderate-intensity groups than in the high-repetition/low-intensity group. In contrast, Hisaeda and colleagues observed similar gains in peak torque and muscle CSA in young women in response to 8 weeks of either high-intensity/low-repetition or high-repetition/low-intensity resistance training (155). The influence of the number of sets performed at each training session on changes in muscle strength and mass in response to resistance training also has been studied. Ronnestad and colleagues demonstrated that 3 sets of lower-body resistance exercise per session was more effective than 1 set in increasing muscle strength and CSA, suggesting that the volume of training may drive the gains in muscle strength and mass (162). In support of this, varying the number of training days per week and the number of training sets performed to control the total volume of work performed per week resulted in similar gains in muscle strength and CSA in young men and women (163). The evidence from these trials suggests that muscle hypertrophy from resistance training occurs in a dose-dependent manner that is primarily dependent on the intensity of the resistance.

As reviewed by Fielding, a number of early studies demonstrated the positive effects of progressive resistance training on muscle mass in healthy older men and women (164). More recent short duration randomized trials have confirmed these initial findings (165-168), and one study has demonstrated that muscle mass can continue to increase in older adults throughout 2 years of resistance training (52).

The influence of age, per se, on changes in muscle mass in response to training also has been investigated. Although resistance exercise training interventions can increase both whole muscle and fiber CSA in older men and women, some evidence indicates that this hypertrophic response is attenuated in old age. Cross-sectional studies of older bodybuilders who had been performing resistance training for 12 to 17 years were reported to have mid-thigh muscle CSAs that were similar to young sedentary controls, suggesting that the ability to stimulate muscle growth is diminished with age (169). In young men and women, the change in mid-thigh CSA after 4 months of high-intensity resistance training is typically 16% to 23 % (157), compared to a 2.5% to 9.0% increase in institutionalized or frail older individuals in response to similar resistance interventions (170-172).

Few studies have directly compared increases in muscle hypertrophy in young and older subjects using a similar standardized training intervention; comparisons across studies are prohibitive due to differences in subject selection criteria, the specific training intervention employed, and the techniques implemented to assess muscle mass. Welle and colleagues reported impaired responses of both knee and elbow flexors, but not knee extensors, after a whole-body resistance training program in older compared to young men and women (173). Hakkinen and colleagues reported a decline in the adaptive response of the vastus lateralis from middle to old age of approximately 40% (174). Lemmer and colleagues reported a significant increase in thigh muscle CSA in both young and older adults following resistance training; the magnitude of the increase was greater in the young (175). Similar results also were observed by Dionne and colleagues following 6 months of resistance training in young and older non-obese women (176). In contrast, resistance training studies of similar intensity and duration also have been reported to generate similar changes in thigh CSA in young and old (160;177). These findings suggest that progressive resistance training-induced increases in muscle mass can occur in older individuals, but that the magnitude of the response may be attenuated, particularly in the oldest old.

Whether the anabolic response to resistance training among older adults is sex-specific remains equivocal. Several studies have reported similar increases in muscle mass in older men and women in response to resistance training (52;160;178;179). In contrast, men were found to have larger increases than women in muscle volume after 9 weeks of high-intensity resistance training (177) and larger increases in fat-free mass after 12 weeks of high-intensity resistance training (180). At the cellular level, Bamman and colleagues found a greater degree of hypertrophy of both type I and II fibers in older men than in older women in response to 26 weeks of high-intensity resistance training (181). However, in contrast to these reports, Hakkinen and colleagues found a smaller increase in muscle CSA in older men than in older women (174). Despite some lack of agreement, the majority of studies evaluated suggested that sex plays a relatively small role in the magnitude of the hypertrophic response to resistance exercise training in older adults.

Physical Activity and Strength

Several studies have documented gains in strength as a direct result of resistance training regimens throughout the lifespan (182;183). In young men, a 2-week isokinetic resistance training program increased isokinetic and isometric quadriceps muscle peak torque at both 60 and 240 degrees (184). In another study of men, a 12-week high-intensity resistance training program resulted in an increase in isokinetic concentric (quadriceps) knee extension strength at a velocity of 30 degrees and eccentric (hamstring) knee joint strength at velocities of 30, 120 and 240 degrees (185). The hamstring/quadriceps ratio also increased. A dynamic resistance training protocol of similar duration resulted in isometric torso rotation strength gains in men and women who exercised twice weekly for 12 weeks (186). Significant gains in both upper- and lower-body strength have also been reported for longer studies (6 months) (138). Although the preferential mode for strength gains has been dynamic resistance training (139;187;188), with inclusion of some amount of eccentric contractions (189), some studies indicate that other modes also may be effective, including nordic training (190), circuit weight training (153), balance training (191), and a combination of strength and endurance or endurance-only protocols (188;192).

In middle-aged men and women subjected to short-duration physical activity interventions, strength gains also have been observed after progressive resistance (150), endurance (193), and multi-modal aerobic/weight (194) training protocols. Gains in strength are evident in longer duration studies (4 to 6 months) in this age group (195;196), and further demonstrate that greater gains in strength begin to occur after 8 weeks of a combined resistance and endurance exercise protocol (196).

In older adults, investigators have used relatively long duration (4 to 12 months) resistance training alone (142;143;145) or in combination with endurance training (144;146;197-199), endurance/balance (200), or endurance/strength/balance/coordination/flexibility (201) regimens to successfully increase strength in an effort to counteract the late-life decline in physical functioning. Although resistance training induces muscle strength gains, functional-task exercises may be more effective at counteracting declines in function (202). It has been suggested that gains in isometric and dynamic muscle strength (199) and in isokinetic muscle strength (145) are associated with improved physical functioning. However, the gains in strength may be muscle-specific and translate into improvements only in select parameters of physical functioning, as indicated in both long- (146;203;204) and short-duration exercise interventions (205). The results of these studies are in agreement with a large systematic review (206) of 62 RCTs of resistance training in older men and women (older than age 60 years), which found that resistance training increased muscle strength and had a modest significant effect on some measures of physical functioning (e.g., gait speed).

Strength gains also have been reported for shorter (8 to 12 week) duration studies of older adults. These studies have employed dynamic training (179;207), exclusively eccentric resistance training (147), an integration of resistance, endurance and balance types of activities (208-210), or endurance-only activities (211). A progressive resistance training protocol in older adults resulted in a linear increase in dynamic strength at different time points of a 12-week study (212). Other intervention paradigms for functional improvements have been explored. In an 8-week comparison between a combined resistance training/functional training regimen (1 day per week of each) and resistance training only

(2 days per week), both programs resulted in significant gains in dynamic strength (213). However, others report a dose-response relationship between high-intensity progressive resistance training and functional capacity that may explain the preponderant use of this type of resistance training (145;214). Gains in strength also occur with low- (215) and variable-intensity resistance training (6 months) (216;217).

Physical Activity and Muscle Power

Although physical activity interventions that increase or maintain muscle strength have important health implications, emerging evidence suggests that muscle power (the rate at which muscle force can be generated) may play a more important role in functional independence and fall prevention, particularly among older adults. Muscle power has been shown to decline more precipitously with aging than does dynamic and isometric strength (218). Lower extremity muscle power also is a strong predictor of physical performance, functional mobility, and risk of falling among older adults (219;220). Muscle power has been found to be inversely associated with self-reported disability status in community-dwelling older adults with mobility limitations (221;222) and is a better discriminator of mobility limitations than muscle strength (220).

Most trials that have evaluated the effects of progressive resistance training on muscle strength and mass have traditionally involved relatively slow movement velocities. Some of these have examined changes in lower extremity power output. In a study of nursing home residents, progressive resistance training resulted in an increase in muscle strength of more than 100%, but only a 28% increase in stair climbing power, suggesting a disproportionate and specific rise in strength versus power with traditional resistance training (171). Skelton and colleagues also examined changes in peak leg extensor power in response to 12 weeks of traditional resistance training in older women (223). They observed increases in strength of 22% to 27% with a non-significant increase in leg extensor power. A randomized trial by Joszi and colleagues also noted a modest improvement (30%) in leg extensor power in response to 12 weeks of progressive resistance training in healthy older men and women (224). More recently, Delmonico and colleagues examined the effects of moderate-velocity resistance training on changes in peak power in older men and women (225). They observed similar changes in absolute peak power in response to 10 weeks of resistance training in both older men and women. However, the relative improvements in peak power were greater in women (16%) compared to the men (11%). Similar results have also been reported by Newton and colleagues employing a “periodized” resistance training intervention in healthy young and older men (226). These studies suggest that traditional slow velocity resistance training results in minimal improvements in peak power, that adaptations may be sex-dependent, and that resistance training performed at relatively slow velocities may lack the specificity to improve peak power, particularly in older individuals.

Early randomized trials that examined high-velocity resistance training to increase muscle power in older subjects compared the effects against walking exercise (227), slow velocity resistance training (228), or slow velocity isokinetic training, (229). In general, these studies all demonstrated that interventions designed to maximize muscle power are feasible, well tolerated, and can dramatically improve lower-extremity muscle power in healthy older men and women and older women with self-reported disability. Earles and colleagues reported a 50% to 141% increase in leg power in older women and men following 12 weeks of high-velocity resistance training in combination with moderate-intensity non-resistance exercise compared to a structured walking program (227). Fielding and colleagues compared high-velocity lower-extremity resistance training with traditional slow-velocity resistance training in older women with self-reported disability (228). They observed an 84% greater increase in leg press power in the high-velocity training group. Similar results were reported by Signorile and colleagues in healthy older men and women in response to 12 weeks of high-velocity isokinetic training (229). All of these studies employed high-velocity training at a relatively high external resistance. Only one study to date has examined high-velocity training at varying levels of external resistance (measured as a percent of the 1 RM) (230). Older adults were randomized to 12 weeks of high-velocity resistance training at 20%, 50%, or 80% of 1 RM. Peak power output improved similarly across all training intensities, suggesting that speed of movement is a key factor in generating improvements in power output.

A small number of studies have evaluated different types of exercise interventions that did not depend on specific resistance training equipment or isokinetic dynamometry, but emphasized explosive power. These have included modified calisthenics and plyometric (i.e., jumping) exercises (231), stair climbing (232), and weighted-vest exercise (233). Bean and colleagues compared 12 weeks of a weighted stair climbing program (i.e., stair climbing while wearing a weighted vest) to a walking program in older adults with baseline mobility limitations (232). When compared with walking, the stair climbing intervention increased leg power by 17% with a corresponding 12% increase in stair climbing power. The same group also examined the effects of a program of weighted vest exercise performed at a high velocity (InVEST) compared to a slow-velocity training program (233). Lower-extremity power and chair rise time were increased more in the InVEST group. Surakka and colleagues examined the effects of a group exercise intervention that consisted of leg and trunk exercise that emphasized both strength and power training (231). They observed that the explosive power training intervention resulted in improved perceived fitness compared to non-exercising controls. These studies confirm that several types of exercise programs that can be performed at high velocity can improve muscle power and improve physical functioning.

A few studies have evaluated the influence of power training on changes in physical functioning in older adults (234-237). Sayers and colleagues compared 16 weeks of slow-velocity resistance training to high-velocity power training in older women with self-reported disability (234). They noted significant improvements in dynamic balance and stair climbing performance in both groups, but no differential effects of the two programs. Recent studies have evaluated low-resistance (40% to 60% 1 RM) high-velocity power training on measures of physical functioning (235-237). Orr and colleagues reported improvements in measures of dynamic balance in older women and men in response to lower-intensity power training when compared with a no-exercise control group (236). Both Miszko and colleages and Bottaro and colleagues. found that lower-intensity power training improved physical functioning composite scores when compared with traditional slow-velocity resistance training (235;237).

Summary

Exercise interventions targeted at improving lower-extremity muscle power in the elderly have been well-tolerated, safe, and effective. Improvements in muscle power were generally greater with interventions that emphasized high- versus low-velocity resistance training. In addition, emerging evidence indicates that higher-velocity, lower-intensity resistance training may improve physical functioning in older adults to a greater extent than traditional slow-velocity resistance training.

Overall Summary

As this chapter amply demonstrates, physical activity has many benefits for musculoskeletal health (for a detailed summary of these benefits, see Table E.1 in ***Section E: Integration and Summary of the Science***). Briefly, physical activity is inversely associated with risk of hip and spine fracture. Exercise training can increase, or slow the decrease, in spine and hip BMD, and can increase skeletal muscle mass, strength, power, and intrinsic neuromuscular activation. In the absence of major joint injury, regular moderate-intensity physical activity does not appear to promote the development of OA. In fact, physical activity may provide protection against the development of OA, but there is limited evidence for this. In adults with OA, participation in moderate-intensity, low-impact physical activity has disease-specific benefits (e.g., pain, function, quality of life).

The musculoskeletal benefits of physical activity have been observed in adult women and men across a wide age range, but information on race and ethnic specificity is lacking. Moderate evidence supports a dose-response association of volume of physical activity with hip fracture risk, and muscle mass and strength increase in an exercise intensity-dependent manner. High-intensity and/or high-velocity resistance exercise may be particularly effective in increasing BMD and muscle strength and power. Endurance exercise, even when high-intensity in nature, has little effect on muscle mass and strength, but may preserve BMD if the activities are weight-bearing. In the absence of major prior joint injury, regular moderate- and vigorous-intensity physical activity in amounts that are commonly recommended for general health benefits does not appear to increase the risk of developing OA.

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Part G. Section 6: Functional Health

Introduction

This chapter reviews evidence related to the effects of physical activity on improving functional health and/or preventing disability in middle-aged and older adults. Background information is provided, followed by an assessment of the evidence related to 3 questions about possible health benefits of physical activity.

Conceptual Model and Terminology

The term "disability" has been defined in several different ways in scientific models of disability (1;2). In this chapter, "disability" is used as an umbrella term to refer to deficits in overall health that affects a person's ability to do tasks of everyday life. That is, disability is the other side of the coin of health — a reasonably (though not perfectly) healthy person has a lot of health, but also a little disability. Measures of physiologic impairment, functional limitations, and role limitations assess the status of basic aspects of the disablement process.

A thorough discussion of the existing conceptual frameworks used to model and describe the disablement process is beyond the scope of this discussion. However, 3 basic concepts, which are included in several models of disability, are often used when discussing this process, and they provided a conceptual foundation for the Functional Health subcommittee's evidence review and deliberations (1;2).

- *The capacity of the physiologic systems of the body* (which depends upon the status of physiological functions and anatomical structures). We refer to this concept as "physiologic capacity," and loss of physiologic capacity is referred to as "physiologic limitation." Examples of physiologic capacity relevant to this section include measures of physical fitness such as aerobic power (VO_{2max}) and muscle strength. A recent review by Paterson and colleagues provides evidence that physical activity programs improve physiologic capacity in older adults (3).

- *The capacity of a person to perform a task, activity, or behavior in a controlled environment that neither enhances nor impairs behavioral abilities.* We refer to this concept as "functional ability," and loss of functional ability is referred to as "functional limitations." Examples of functional abilities include ability to walk at a normal speed on a flat surface, and ability to climb a typical flight of stairs.

- *The capacity of a person to perform a task, activity, or behavior in his or her actual environment, so as to fulfill the roles a person assumes in life.* We refer to this concept as "role ability," and loss of role ability is referred to as "role limitations." We live in environments that contain physical and social factors that facilitate or impair ability to perform roles. A person who cannot walk several hundred meters cannot perform the task of grocery shopping in a large grocery store and fulfill the role of family food shopper. But he or she can perform the task in a small store or in a store with motorized carts. Measures of role performance include activities of daily living (ADL) and instrumental activities of daily living (IADL) scales.

Another term that is key to this chapter and to the health of older adults is "fall." A fall is defined as unintentionally coming to rest on the ground, floor, or other level lower than one's starting point (4). Falls in older adults can be classified into 3 main groups. About 20% of falls result from an external precipitant, such as being tripped up by a large, rambunctious dog while out for a walk. This type of fall is simply the consequence of an active lifestyle, and not the result of a disablement process. Another 20% of falls are due to a single identifiable cause, such as a drug-related syncope, stroke, or Parkinson's disease. Adults with such falls require diagnosis and specific therapy directed at the single major cause. The majority of falls, though, result from multiple etiological or causative factors interacting that put older adults at risk of falling. This chapter is concerned with the prevention of this type of fall. Characteristically, falls of this type have only minor provocation, such as tripping on a step or loose rug. Epidemiologic studies suggest that decline in muscular strength, speed of reaction, and balance are key factors in fall risk (4;5). It is well documented that older adults with functional limitations are at increased risk for falls and their sequelae, such as fractures of the wrist and hip. Hence, these falls are regarded as a result of the disablement process in older adults.

Functional Health in Middle-Aged and Older Adults

The etiology of disability differs strongly by age. Disease-related disability affecting middle-aged and older adults accompanies well-known, common diseases, such as cardiovascular disease, depression, diabetes, stroke, arthritis, and dementia (6;7). The effects of such diseases on disability are compounded by loss of physiologic capacity due to biologic aging, such as decline in aerobic capacity, muscle strength, and balance (8;9). The models of disability in older adults involve concepts like frailty, where the capacities of multiple physiologic systems are markedly reduced.

In contrast, disability in younger age groups is much less prevalent, is much less likely to be due to such chronic diseases, and is not compounded by declines associated with aging. It involves, for example, developmental disabilities, genetic syndromes, and traumatic injuries. Because of the difference in pathogenesis by age, it is appropriate to separate the evidence review of disability in children and young adults from the evidence review in older adults. This chapter reviews the evidence for older adults.

The Importance of Reducing Disability and Falls in Older Adults

Older adults have the highest prevalence of disability (10) and falls (4) of any age group in the population. Studies consistently show that the prevalence of both major disability and falls increases with age, and is higher in women than men. As the life expectancy of older Americans continues to increase, the burden of disability in older populations is also expected to increase. The Medicare Current Beneficiary Survey (MCBS) is particularly useful for characterizing disability in older adults, as it includes persons living in the community and persons living in long-term care facilities (11). In 2003, the MCBS characterized mobility limitation as difficulty walking a quarter of a mile. In men, the prevalence of mobility disability was 31% for those aged 65 to 74 years, 46% for those aged 75 to 84 years, and 69% for those aged 85 years and older. Corresponding percentages in women were 42%, 57%, and 81% (11). In a community population aged 70 years and older, around one third of people will fall in any 1 year (4). In a recent US survey, approximately 5.8 million persons aged 65 or older fell in the preceding 3-month period (12). Fall rates increase with age and are higher in women than men. Fall-related injuries can have a large adverse effect on functional ability in older adults and can sometimes directly result in death (5;13-15).

Disabilities and falls have a significant impact on the ability of older adults to live independently, and the treatment and management of disability and falls in older adults consume enormous resources involving both medical care and long-term care (16-18). One can hardly overestimate the importance of independent living to quality of life in older adults.

National surveys consistently show that older adults are the least active age group of Americans. For example, national survey data from 2005 show that an average of only 21% of people aged 65 years and older report meeting recommended levels of physical activity, with women reporting slightly less physical activity participation rates than men (19). A recent national survey using an objective measure of physical activity (accelerometers) suggests older adults may be substantially less active than they report on questionnaires (20). If physical activity prevents or delays disability, the majority of older Americans stand to benefit.

Review of the Science

Overview of Questions Addressed

This chapter addresses 3 major questions:

1. In middle-aged and older adults who do not have severe functional or role limitations, does regular physical activity prevent or delay the onset of substantial functional limitations and/or role limitations?

2. In older adults, who have mild, moderate, or severe functional or role limitations, does regular physical activity improve or maintain functional ability and role ability with aging?

3. In older adults who are at increased risk, does regular physical activity reduce rates of falls and fall-related injuries?

Data Sources and Process Used To Answer Questions

The Functional Health subcommittee used the *Physical Activity Guidelines for Americans* Scientific Database as its primary source of literature since 1995 to review all 3 questions (see ***Part F: Scientific Literature Search Methodology,*** for a full description of the Database). The subcommittee then used the reference lists from those papers as well as the collective expertise of its members and consultants to identify additional relevant publications, meta-analyses, and systematic reviews.

Question 1: In Middle-Aged and Older Adults Who Do Not Have Severe Functional or Role Limitations, Does Regular Physical Activity Prevent or Delay the Onset of Substantial Functional Limitations and/or Role Limitations?

Conclusions

Strong, consistent observational evidence indicates that mid-life and older adults who participate in regular physical activity have reduced risk of moderate or severe functional limitations and role limitations. Active mid-life and older individuals — both men and women — have approximately a 30% lower risk of developing moderate or severe functional limitations or role limitations compared with inactive individuals. The observational evidence of benefit is strong for aerobic activity, but limited for other types of activity (muscle-strengthening, balance, and flexibility activities). It should be noted that no randomized controlled trials (RCTs) were available to answer Question 1.

Several important findings from the literature review support this conclusion:

- The results were strongly consistent across studies;

- In studies with repeated measures of physical activity during follow-up, adults who reported regular physical activity at all measurement occasions were at lowest risk of functional limitations; and

- Studies that assessed change in physical activity over time reported that change from lower levels of activity to higher levels of activity over time was associated with reduced risk of limitations.

Introduction

The aging of the American population has led to large numbers of older persons (aged 65 years and older), with a rapidly expanding proportion reaching advanced old age (85 years and older), a category termed the oldest old (21). This population includes large numbers of older adults who have no difficulty or only mild difficulty living independently in the community (11;22). That is, such older adults have no or mild functional limitations and role limitations. Across the population, older adults strongly wish to avoid major functional limitations and major role limitations that would lead to dependent living. Hence, Question 1 asks a primary prevention question: Does physical activity prevent or delay onset of moderate or severe functional limitations and/or role limitations in middle-aged and older adults?

It is theoretically possible to answer this question using a large RCT. The problem is that such trials are extremely difficult and expensive, and to our knowledge such a study has never been done. Analogous to other primary prevention studies regarding lifestyle, such as tobacco or nutrition, information about prevention comes from observational studies, including both prospective and retrospective cohort studies. Cohort studies of physical activity and disability generally use one of 2 approaches. Some studies use a dichotomous measure of disability (e.g., presence or absence of inability to walk 400 meters) as an outcome, and compare rates of incident disability in people with different levels of physical activity. Other studies use a continuous measure of disability (e.g., the Health Assessment Questionnaire-Disability Index) and compare the rate of decline in people with different levels of physical activity (23).

Conceptually, the cohort studies can also be divided into 2 types based upon the population they recruit. A “pure” primary prevention study would include adults and older adults with either no limitations or mild limitations at baseline, and assess whether physical activity prevents or delays onset of moderate or severe limitations. The other approach is to assess whether physical activity prevents severe limitations in a population that includes adults with no, mild, or moderate limitations. Both types of studies exist and were used to address the question.

Given decades of research showing that physical activity in healthy adults (including healthy older adults) improves physiologic capacity and hence functional ability (e.g., ability to walk a mile), one might ask, “Doesn’t this mean physical activity prevents disability?” A response to this question is that the pathogenesis of decline in older adults is complex, with many causal factors and etiologic pathways involving a large number of diseases. The improvement in physical fitness and physical performance is one mechanism by which physical activity can prevent decline. The reduction in the incidence of chronic diseases (e.g., ischemic heart disease, depression, type 2 diabetes) is another mechanism by which physical activity can prevent decline. However, a more meaningful question is whether the net effect of physical activity across all etiologic pathways (only some of which are influenced by physical activity) is sufficient to have a meaningful effect size on the incidence (or rate) of moderate or severe limitations in older adults.

Rationale

The Scientific Database was the primary source of studies for review to answer Question 1. Additional research studies (not in the Database) were identified by review of reference lists of published studies. The subcommittee members and consultants also identified papers for consideration based upon their expertise and knowledge of the field. Information from the articles was systematically abstracted and summarized in the tables and figures accompanying the chapter. The search of studies was limited to studies published between 1995 and 2007. In addition, a supplemental PubMed search was performed to find reviews of the literature between 1990 and 2007.

Specifically, we sought only cohort studies (including both prospective and retrospective studies) that measured the physical activity level of participants at baseline as the exposure variable, and assessed either functional limitations or role limitations during follow-up as an outcome variable. As indicated above, these studies were of 2 types: (1) the study sample at baseline included adults with only no or mild functional limitations or role limitations; and (2) the study sample at baseline included adults with none, mild, or moderate functional limitations or role limitations. We regarded ADL limitation as an indicator of severe role limitations. Studies that examined only the relation between physical fitness and risk of functional/role limitations were not included in the review.

Twenty-eight prospective cohort studies addressed the relation between physical activity and risk of functional limitations and role limitations (23-50). Table G6.A1 provides a summary of the studies. (Table G6.A1, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.) Almost all these prospective cohort studies reported that active adults had a lower incidence of functional and role limitations. Only 4 studies did not find a significant relation between physical activity and risk of functional or role limitations (26;31;43;48). However, statistical power was limited in some of these negative studies, as illustrated by a study where the confidence interval (CI) on one adjusted odds ratio of .91 ranged from .22 to 3.70 (31) and a study where a 23% reduction in risk was not statistically significant (48). Both of the other two studies were not significant at the 0.05 level, but were very close (26;43).

The findings were consistent across different types of outcome measures that included measures of functional limitations as well as role limitations, including measures of mobility, ADL, IADL, measures of overall (“global”) functional and role limitations, and occupational status. In studies that used an odds ratio or hazard ratio to quantify the risk reduction, 19 studies reported at least a 30% lower risk (a ratio or 0.70 or less) when comparing the most active to the least active subgroups of adults. Studies with repeated assessments of physical activity consistently reported that adults who were regularly active during follow-up had the lowest risk of disability (30;32;34;36). The 2 studies that assessed change in physical activity level during follow-up consistently reported that adults who switched from inactive to active during follow-up had a lower risk of limitations than adults who remained inactive (23;48). One study also measured aerobic fitness (using a treadmill test) (32). Although both physical activity and aerobic fitness were each associated with significantly reduced risk of functional limitations over time for both men and women, the aerobic fitness provided even greater risk reduction (OR 0.30) (32).

Dose-Response Pattern

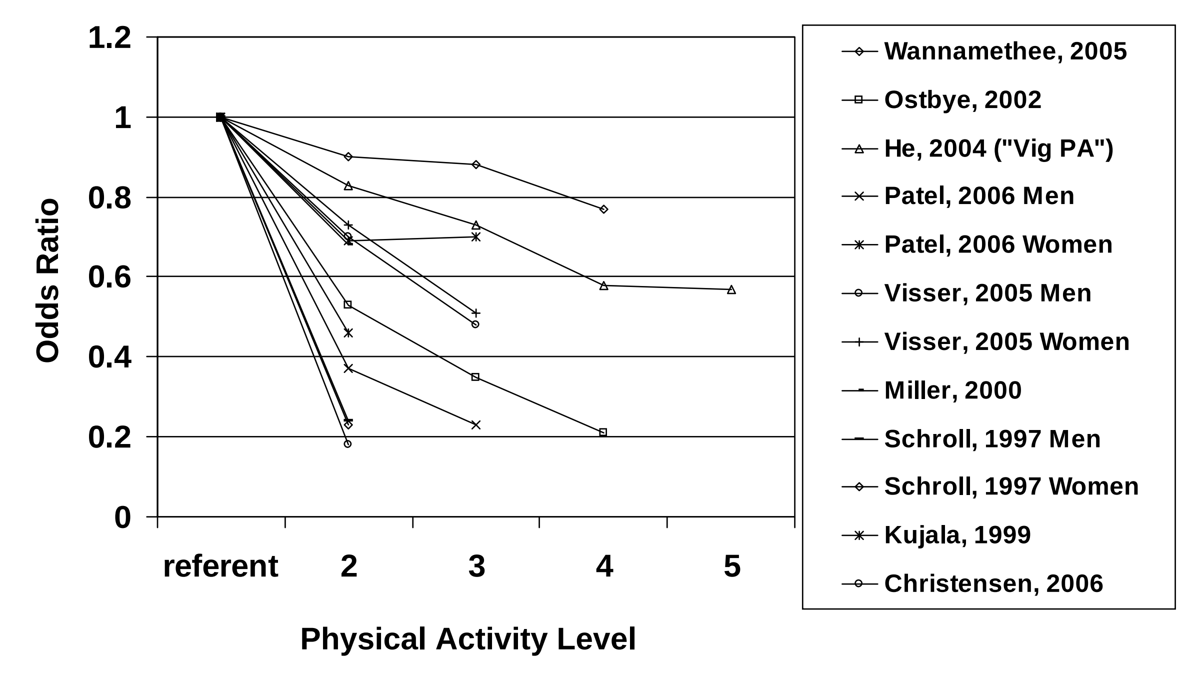
The findings from the prospective cohort studies support a dose-response effect, where greater amounts of physical activity were associated with lower risk of limitations. Figure G6.1 shows data from prospective cohort studies with measures of mobility limitations. Figure G6.2 shows data from studies with ADL, IADL, and/or global measures. When studies reported a statistical test of trend across categories of physical activity, the trend was statistically significant (29;30;32;34;36;37) with one exception where P=0.08 (48).

Because of the diversity in methods used to assess physical activity, it was not possible to reach a conclusion about the amount of risk reduction that occurs from a specific amount of physical activity. However, a reasonable conclusion is that adults who do moderate amounts of activity for the purposes of reducing risk of common chronic diseases also would reduce risk of functional and role limitations.

Generalizability of Findings

The research supports the conclusion that the findings are widely applicable to older adults. Some studies, such as the Longitudinal Study of Aging and the Health and Retirement Study, enrolled nationally representative samples (29;35;36). Many others involved a systematic sample of a specific geographic area within a country, such as a city. About half the prospective cohort studies enrolled samples that included adults aged 85 years and older, thereby providing evidence that the oldest old benefit from physical activity (although most did not analyze data separately for that age group). Most studies enrolled both men and women. Studies that did separate analyses for men and women commonly reported significant benefits for both (28;32;37;40;46). Almost all studies were done in the United States or Europe, though one study (50) was from Taiwan and one study (42) was from Israel. Although the studies did not directly compare the effect of physical activity among different race/ethnic groups, no evidence suggested that effects of physical activity would not occur in all race/ethnic groups. It could not always be ascertained with certainty, but it appeared about half the studies enrolled adults with no or mild limitations, and about half the studies enrolled adults with no, mild, or moderate limitations. We located only one study that included objective measures of both physical activity and of functional limitations (25). Four studies measured some outcome related to physical fitness or functional ability in addition to physical activity and functional limitations (25;32;38;40).

Figure G6.1. Prospective Cohort Studies With Measurement of Mobility Limitations

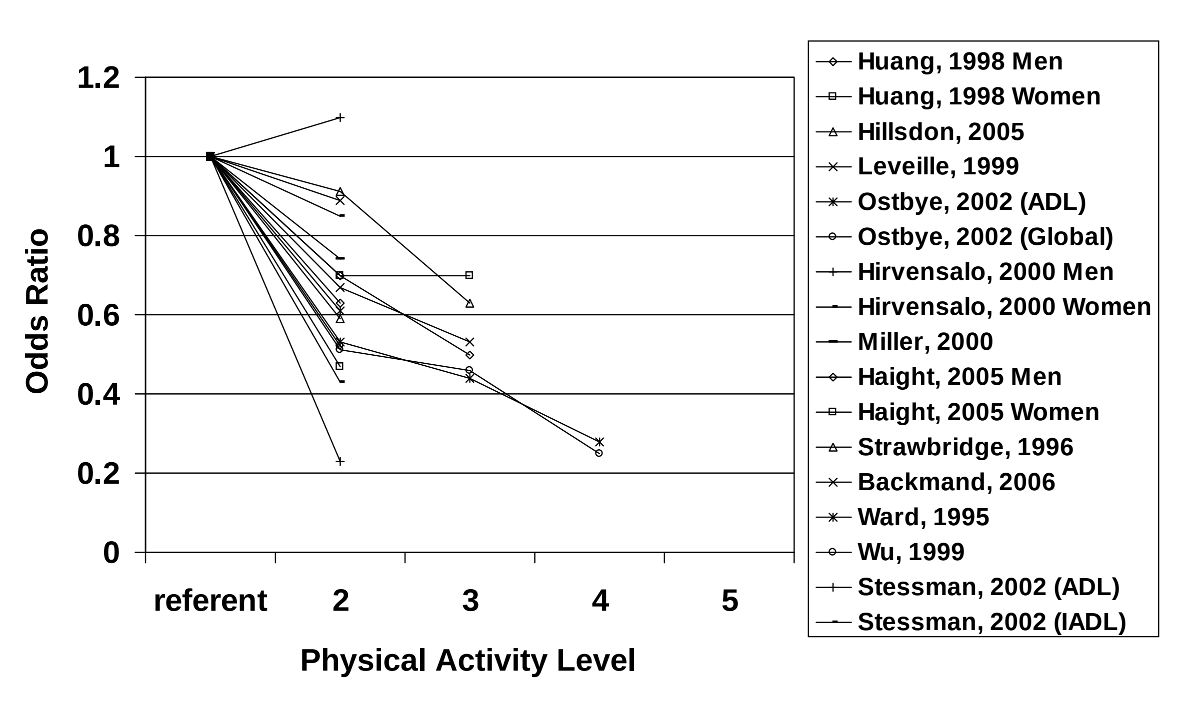


Legend: The figure shows the reported odds ratio for each category of physical activity (PA), with the lowest category of PA assigned as the referent category. For example, the Wannamethee study had four categories of PA, with category 1 (the referent) assigned to those with the lowest level of PA, category 4 assigned to those with the highest activity level, with all categories forming an ordinal scale.

Figure G6.1. Data Points

	Referent	2	3	4	5
Wannamethee et al., 2005 (48)	1	0.9	0.88	0.77	
Ostbye et al., 2002 (36)	1	0.53	0.35	0.21	
He et al., 2004 ("Vigorous PA") (29)	1	0.83	0.73	0.58	0.57
Patel et al., 2006 Men (37)	1	0.37	0.23		
Patel et al., 2006 Women (37)	1	0.69	0.7		
Visser et al., 2005 Men (46)	1	0.7	0.48		
Visser et al., 2005 Women (46)	1	0.73	0.51		
Miller et al., 2000 (35)	1	0.68			
Schroll et al., 1997 Men (40)	1	0.24			
Schroll et al., 1997 Women (40)	1	0.23			
Kujala et al., 1999 (33)	1	0.46			
Christensen et al., 2006 (26)	1	0.18			

Figure G6.2. Prospective Cohort Studies With Measures of ADL, IADL, and Global Outcomes



Legend: ADL, activities of daily living; IADL, instrumental activities of daily living. The figure shows the reported odds ratio for each category of physical activity, with the lowest category of physical activity assigned as the referent category. For example, the Huang study had three categories of physical activity, with category 1 (the referent) assigned to those with the lowest level of physical activity, category 3 assigned to those with the highest activity level, with all categories forming an ordinal scale.

Figure G6.2. Data Points

	Referent	2	3	4	5
Huang et al., 1998 Men (32)	1	0.7	0.5		
Huang et al., 1998 Women (32)	1	0.7	0.7		
Hillsdon et al., 2005 (30)	1	0.91	0.63		
Leveille et al., 1999 (34)	1	0.67	0.53		
Ostbye et al., 2002 (ADL) (36)	1	0.53	0.44	0.28	
Ostbye et al., 2002 (Global) (36)	1	0.51	0.46	0.25	
Hirvensalo et al., 2000 Men (31)	1	1.1			
Hirvensalo et al., 2000 Women (31)	1	0.85			
Miller et al., 2000 (35)	1	0.74			
Haight et al., 2005 Men (28)	1	0.63			
Haight et al., 2005 Women (28)	1	0.47			
Strawbridge et al., 1996 (43)	1	0.59			
Backmand et al., 2006 (24)	1	0.89			
Ward et al., 1995 (49)	1	0.61			
Wu et al., 1999 (50)	1	0.52			
Stessman et al., 2002 (ADL) (42)	1	0.23			
Stessman et al., 2002 (IADL) (42)	1	0.43			

Limitations

The conclusions for Question 1 have several caveats. First, because all of the studies in the evidence base were observational epidemiologic studies with no RCTs, the data cannot prove causality of effect. Some concern exists that the prospective cohort studies could not adequately adjust for confounders and may have overestimated the effect. Healthy people are more physically active than are people with health conditions, and adjusting for all health status differences between physically active and sedentary persons is not possible in these studies. However, the consistency of evidence does support a cause-and-effect relation between physical activity and lower risk of functional and role limitations. In addition, plausible biological mechanisms — demonstrated in RCTs — exist for physical activity to improve physiologic capacity (e.g., aerobic power, strength, balance) and functional ability in older adults (see Question 2). These are all important factors in the causal pathway toward disability.

Second, although evidence indicates that regular aerobic activity prevents functional and role limitations, evidence of a beneficial effect of muscle strengthening activities, balance activities, and flexibility activities is insufficient. Two additionally reviewed studies analyzed measures of leg strength, with one reporting that higher leg strength reduced risk of limitations (51) and another essentially reporting no association (40).

Third, although the literature provides sufficient evidence of a dose-response effect (i.e., the more physical activity, the greater the preventive effect), it is difficult to make statements about the amount of physical activity required for substantial preventive effect. It was common for studies to use simple measures of self-reported physical activity (e.g., frequency and duration of walking activities), but not to provide information of the validity of the measurement method. All the studies but one (25) relied upon self-report measures of physical activity and most used self-report measures of functional and role limitations. Additional studies that use objective measures of physical activity and objective measures of functional ability are needed.

Finally, data are insufficient to determine whether the preventive benefits of physical activity differ by race or ethnic group. Some studies enrolled representative samples of the US older adult population, but few studies directly compare the effects of physical activity across race or ethnic groups.

Question 2: In Older Adults Who Have Mild, Moderate, or Severe Functional or Role Limitations, Does Regular Physical Activity Improve or Maintain Functional Ability and Role Ability With Aging?

Conclusions

Modest evidence indicates that regular physical activity in older adults with existing functional limitations improves functional ability. Due to the lack of well-designed intervention trials, only limited evidence is available to conclude that physical activity in older adults with existing functional limitations improves or maintains role ability with aging.

Most of the physical activity interventions included both aerobic (especially walking) and muscle strengthening activities, with fewer interventions using only a single type of activity. For this reason, most evidence reflects a pattern of physical activity that involves periods of 30 to 90 minutes of moderate to vigorous physical activity, on 3 to 5 days per week, in which most of this time is devoted to aerobic activity and muscle strengthening activity and with a shorter amount of time spent on other forms of activity, such as flexibility. When it was possible to determine the amount of time spent just on aerobic activity (mostly walking), it usually varied from 60 minutes per week to 150 minutes per week. Because of low baseline fitness levels in older adults, "relative intensity" should be used for determining exercise intensity instead of absolute intensity. Evidence is limited that physical activity levels less then described above provide some benefit.

Introduction

Some older adults already have functional limitations and role limitations. However, prevention of further decline is still relevant for these older adults and this is the focus of Question 2. In people with existing diseases or limitations, concern always exists that the disease processes are so advanced that they are difficult to influence. Question 2 can be thought of as asking whether it is "too late" for people with existing limitations to benefit from physical activity.

Both RCTs and observational studies have been conducted to address Question 2. The RCTs address whether the rate of change ("decline") in functional or role limitations differs between a control group and a physical activity group. The observational studies and RCTs provide complementary information, in that observational studies can address the effects of years of regular physical activity (though residual confounding, resulting from differences between people who choose to exercise versus those who do not that cannot be fully adjusted for, is a threat to their validity), while few existing randomized trials have studied more than 12 months of regular physical activity (but randomization greatly reduces the risk of confounding).

Rationale

The sources of research studies was the same as for Question 1 – studies published between 1995 and 2007, relying mainly on the Scientific Database for locating the studies. The Functional Health subcommittee included only RCTs and prospective cohort trails that included adults aged 60 years or older with functional limitations and role limitations and recruitment of 25 subjects or more. We excluded papers if they focused on a specific disease (e.g., dementia) or subjects who were hospitalized at the start of the trial. We excluded studies in healthy adults with no limitations. We included only studies whose primary purpose was to determine whether physical activity affected functional health. Some of these studies recruited only participants with mild to moderate functional limitations, and some recruited a mix of participants with no, mild, or moderate limitations. Because of incomplete information on functional ability in participants in many studies, we could not always ascertain the range of functional ability of the study sample. It should be noted that the subcommittee did not review studies focusing on arthritis and functional health, as this topic is covered in ***Part G. Section 5: Musculoskeletal Health.***

Fourteen trials were reviewed to answer this question: 12 RCTs (52-63) (Table G6.A2) (Table G6.A2, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.) and 2 prospective cohort studies (31;41) In addition, 4 review papers considered this issue (64-67). The sample size in the RCTs ranged from 39 to 486 subjects. The prospective cohort studies had samples of slightly more than 1,000 subjects (31;41). All of the subjects in these studies were older adults aged 65 years or older. All of the RCTs recruited subjects who were sedentary. The baseline health status of the subjects varied. Eight of the RCTs recruited people with functional limitations (52;55;57;58;60-63); 4 of the trials recruited subjects both with and without functional limitations (53;54;56;59). In most of the studies, the subjects were older adults who lived in the community. Only one study enrolled adults living in a residential-care facility (55).

All but one of the randomized trials used multimodal interventions that included a mixture of aerobic activity, balance training, strength training, and/or physical therapy guided functional training. One study used a single intervention of muscle-strengthening or power activities (60). The format of the interventions varied. Some of the interventions were supervised group sessions held in community settings, some took place in the home (supervised or unsupervised), and still others were a mixture of the two. The frequency and duration of the interventions also varied, though the majority of interventions took place 3 to 5 days per week and lasted between 40 and 90 minutes. The length of the interventions ranged from 1.5 months to 18 months.

There are no universally agreed upon “functional ability” outcomes. For this reason, it was very difficult to review and compare the literature. The Subcommittee therefore deliberately decided to be liberal in selecting the criteria of outcomes related to functional ability. The outcomes reported in the reviewed trials included, among others, gait speed, timed walking tests, functional reach, and “get up and go,” as well as performance on observational functional health instruments such as the Short Physical Performance Battery (SPPB), Physical Performance Test (PPT), McArthur Battery Scores, and functional obstacle course. The subcommittee also reviewed trials that recorded self-reported functional health using instruments such as the Functional Status Questionnaire and the SF-36 (the emotional health SF-36 subscale was not reviewed). ADLs and IADLs were measured using a variety of standardized questionnaires. All of the trials demonstrated an improvement in one or more functional ability outcomes. A reasonable question is whether the magnitude of change seen in these trials on functional ability can affect role limitations or ability. Most trials were underpowered to examine this question and did not measure ADLs or IADLs.

The most recent, and one of the largest trials to date to address physical activity and functional ability, is the Lifestyle Interventions and Independence for Elders Pilot (LIFE-P) trial (62). LIFE-P examined the effects of a mixed-modal physical activity intervention on functional performance. The trial included 424 men and women aged 70 to 89 years who had mild to moderate functional limitations at baseline. The participants were randomized to either a multi-modal exercise group or an attention-matched control group. The people in the exercise group participated in a combination of aerobic, strength, balance, and flexibility exercises (with primary emphasis on walking). The muscle strengthening and flexibility exercises focused on lower body extremity exercises. Subjects spent the first 8 weeks (adoption) attending 3 supervised center-based sessions per week. The sessions lasted 40 to 60 minutes each. During the next 4 months (transition), the number of center-based sessions was reduced to 2 times per week, and home-based endurance/strength/flexibility exercises were started (3 or more times per week). The subsequent maintenance phase consisted of the home-based intervention, with optional once to twice per week center-based sessions. The primary goal was to walk 150 minutes per week at a moderate intensity. The intervention also included a strong behavioral component, with the participants receiving 10 group-based behavioral counseling sessions during the first 10 weeks. The average walking time during the maintenance phase was 138 minutes per week; average frequency of moderate physical activity per week was 6.4 times per week at 6 months and 5.1 times per week at 12 months. The people in the attention-control group participated in a health education program. In this trial, adverse events were carefully monitored and each group had similar rates of non-serious and serious adverse events. The LIFE-P trial found that, compared to those in the health education program, the people who participated in the exercise intervention were able to significantly improve both their SPPB and 400-meter walking speed during the 1.2-year intervention ($P<0.001$). This pilot study also showed a trend toward a reduction in the risk of major mobility disability (i.e., inability to walk 400 meters) (hazard ratio = 0.71, CI 0.44 to 1.20) although this pilot study was not powered for this outcome. In another recent large study (n=486) in very old men and women (85 years or older) in Finland, a multi-dimensional 17-month intervention that included exercise (walking, group exercises, and/or home exercises) demonstrated no improvements in ADLs. However, mobility score and balance improved more in the intervention group than in controls (58).

The Women's Health and Aging Study (WHAS) was a longitudinal cohort study that met the criteria for inclusion in this review (41). In this study, 1,002 women aged 65 years and older who had functional limitations at baseline were recruited. Of the 800 functionally limited women who could walk unassisted at baseline and were alive and contacted 1 year later, 226 (28%) walked regularly at least 8 blocks per week. These women exhibited better health and functioning than did non-walkers. In addition, walkers were 1.8 times more likely (95% CI 1.2 to 2.7; $P=0.002$) to maintain reported walking ability and showed less decline in customary walking speed and functional performance score over the follow-up period. A Finish cohort study of 1,109 men and women (aged 65 years or older) were followed for 8 years (31). Subjects at baseline were either functionally impaired or had no functional limitations and all subjects (regardless of functional status) were categorized as being sedentary or active. Among those who were impaired at baseline, those who were active had a reduced risk of becoming dependent (role limitation) over the 8-year follow-up.

Four relevant systematic review papers focused on different aspects of functional health (64-67). The most recent review was that of Baker and colleagues (64). The authors limited their review to only randomized controlled exercise trials of at least 3 modalities of training, e.g., strength, aerobic, and balance. The 3 modes of training had to be conducted concurrently. Many interventions have focused on these 3 modes of exercise in combination because older adults who are at risk of functional limitations generally have deficits in these areas. Therefore, it makes sense to target these areas with a multi-modal exercise program. In addition, the review only considered trials with subjects aged 60 years or older. The authors systematically reviewed 15 studies totaling 2,149 subjects. A low effect size was seen for changes in dynamic strength (mean 0.41, range −0.08 to 1.67), and balance improved in only 6 of the 11 studies that included balance as an outcome (the positive effect on reducing falls is reported in Question 3). The authors concluded that the effect size for functional health changes were minimal when all studies were considered. The authors gave a number of reasons for the low effect size of these multi-modal interventions on functional health. One reason was that a ceiling effect may have prevented further improvement in some functional measures, as many of the trials reviewed included subjects with high baseline functional ability. However, the authors posited that the most likely reason for a small effect size was that the intensity and duration of any given modality was not robust enough to elicit meaningful physiologic changes that could affect functional health. The authors of the review suggest that more evidence is needed to establish whether multi-modal exercise at adequate volumes and intensity is feasible and effective in older populations and whether multi-modal interventions are in fact more effective than single mode interventions. The LIFE-P study described above and the study of Binder and colleagues (52) were exceptions to the findings in this review, as these 2 studies did show better outcomes. This is most likely due to the size of these studies, the functional limitations of the subjects at baseline, robust interventions, objectively measured primary outcomes, and the length of the trials.

Keysor and Jette reviewed 31 studies (28 RCTs and 2 quasi-experimental trials) that examined the impact of various physical activity programs on functional activities and/or disabilities among older adults (65). The mean age of subjects was older than age 60 years, although the trials had no lower age limit for inclusion. Sample sizes of the trials ranged from 24 to 439. The most consistent positive effects of exercise were observed in strength, aerobic capacity, flexibility, walking, and balance, with more than half of the trials that examined these outcomes finding positive effects. Of the studies that examined physical, social, emotional, and overall disability outcomes, most found no improvements. Only 5 of the studies in the review reported reduced physical disability. The authors of the review note that methodological issues may be one of the main limitations in the studies that have examined disability outcomes. In another critical review by Keysor in 2003, the overall conclusions were similar (67). Exercise increases muscular strength and aerobic capacity and improves functional ability. However, it is less clear whether physical activity or exercise prevents or minimizes disability.

The fourth review considered for Question 2 was that of Latham and colleagues (66). In this review, the authors focused solely on progressive resistance strength training interventions trials in older adults (aged 60 years and older). The authors identified 62 trials with a total of 3,674 subjects. The authors noted that most studies were of low quality due to poor design, small numbers, unclear randomization schemes, and other problems. Progressive resistance strength training showed a strong positive effect on strength and the training had a modest effect on some measures of functional limitations such as gait. No evidence of an effect was found for physical disabilities in the 14 studies that reported disability outcomes. It is important to note that the main objective of most of the trials in the review was not to reduce disability. (Muscle strengthening activities are addressed more fully in ***Part G. Section 5: Musculoskeletal Health.***)

Sex and Race/Ethnicity

Men and women have been represented about equally in the exercise trials that were reviewed. Although not systematically tested, no evidence appears that older men and women respond differently to exercise interventions focusing on functional health. Many of the studies demonstrated that men had higher physiologic and functional status than women at any given age. No trials reviewed for this question had adequate numbers of non-whites to do sub-analyses to determine whether responses to exercise differ among racial or ethnic groups.

Comparison to Current Guidelines

Current recommendations from the American College of Sports Medicine (ACSM) and the American Heart Association (AHA) recommend that older adults participate in moderate to vigorous intensity aerobic activity, muscle strengthening activity, and activities to maintain or increase flexibility; balance exercises are recommended for older adults at risk of falls (68). Out of the 12 randomized trials reviewed, 8 roughly met the recommendations outlined by ACSM/AHA (52;54;56;57;59;61-63). The LIFE-P Trial and the studies by Binder and colleagues and Nelson and colleagues saw robust improvements in functional ability. The study of Binder and colleagues also saw an improvement in aerobic capacity (VO_{2max}). The effects of the interventions on functional ability were not as robust in the studies of Cress and colleagues and King and colleagues. This is most likely due to the fact that the subjects in these two trials had higher functional ability at baseline, as both studies recruited older subjects with and without functional limitations at baseline. It is important to note that muscle strength and aerobic capacity (VO_{2max}) improved in the study of Cress and colleagues demonstrating an improvement in physiologic capacity that was accompanied by modest improvements in functional ability. Also of note, the study of King and colleagues used “flexibility” exercises as their attention-control group (57). The subjects in this group had greater reductions in self-reported bodily pain. This is one of the only studies to investigate flexibility exercises.

Limited evidence suggests that functional health in older adults can be improved with less frequent physical activity than recommended by the ACSM, as the other 4 trials reviewed used interventions below this threshold and each demonstrated some improvements in function ability (53;55;58;60).

Question 3: In Older Adults Who Are at Increased Risk, Does Regular Physical Activity Reduce Rates of Falls and Fall-Related Injuries?

Conclusions

Clear evidence demonstrates that participation in physical activity programs is safe and can effectively reduce falls in older adults at elevated risk of falls. Limited evidence indicates that physical activity programs reduce injurious falls in older adults. Currently, the evidence is strongest for physical activity interventions that include muscle strengthening and balance training activities in combination with aerobic activities, especially walking. In addition, moderate, but inconsistent, evidence shows that tai chi exercise or balance-only training programs provide benefit.

Most of the interventions reviewed included a pattern of physical activity that involves 3 times per week of balance and moderate intensity muscle-strengthening at 30 minutes per session, with additional encouragement to participate in moderate-intensity walking activities 2 or more days per week for 30 minutes a session. It was difficult to ascertain an optimal dose for tai chi, as risk reduction was seen in one trial with as little as 1 hour per week, whereas other trials had greater frequency (e.g., 3 days per week). Limited evidence suggests that physical activity levels less than those described above provides some benefit.

Introduction

It is not until age-related decline in muscle strength and stability reaches a critical threshold that the risk of falls and functional decline threaten independent living. This threshold occurs when the daily activities of life are at or near the limit of a person's physiologic capacity (e.g., muscle strength and balance). Minor perturbations may precipitate the fall, but it appears from epidemiologic studies that the underlying cause is the person's critically compromised physical fitness — particularly strength and balance (69). Theoretically therefore, only small improvements in strength and balance may be needed to lift the person above the threshold where daily living activities are hazardous.

Numerous RCTs of interventions to prevent falls have been conducted in older adults. A multi-component approach is now recommended to address factors that increase fall risk (69), and so trials now commonly test multi-component interventions. These components include removal of environmental hazards (e.g., loose mats), medical treatment (e.g., eliminating drugs that increase fall risk), and physical activity. However, it is difficult to deduce *post-hoc* which elements of a multi-component intervention are efficacious, so the literature on multi-component interventions was not reviewed.

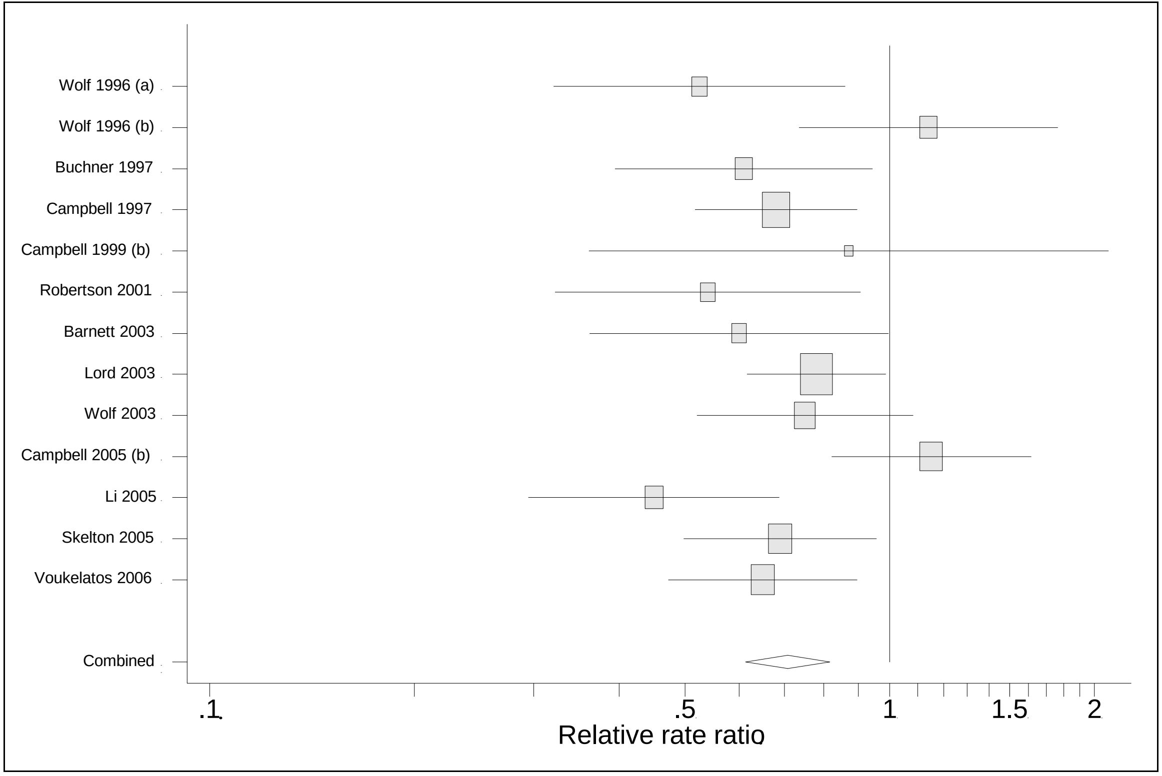
However, some RCTs have focused on physical activity as the sole intervention to prevent falls and fall injuries. As discussed below, these trials typically test a multi-modal exercise intervention involving some combination of aerobic (e.g., walking), muscle-strengthening, balance, and flexibility activities, or they have tested tai chi.

Rationale

Using the *Physical Activity Guidelines for Americans* Scientific Database and consultant suggestions, the subcommittee identified 8 systematic reviews or meta-analyses addressing physical activity and falls (70-77). When necessary, the subcommittee reviewed the original research papers referred to in the meta-analyses and reviews to ascertain study details regarding subject population and physical activity interventions.

The meta-analysis by Campbell and Robertson is the most recent analysis that addresses physical activity and falls (70). The authors employed stringent inclusion criteria for the analysis: 1) all studies were RCTs; 2) all participants were aged 60 years or older or had a mean age older than 70 years; 3) the majority of the participants lived independently in the community; 4) fall events were recorded prospectively; 5) follow up lasted at least 6 months; 6) at least 70% of the participants completed the trial; 7) all falls during the trial for at least 50% of the participants were included in the analysis; and 8) a relative rate ratio with 95% CI comparing the number of falls in the intervention group and the control group were recorded. Twelve physical activity trials met the inclusion criteria for the analysis (one of the trials compared 2 different exercise interventions to controls (78). The pooled rate ratio was 0.71 (95% CI 0.61 to 0.82; $P<0.001$), indicating that physical activity reduces risk of falls (see Figure G6.3 and Table G6.A3) (Table G6.A3, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/.) The trials included strength and balance training (79-85), computerized balance training (78), tai chi (78;86-88). One study included endurance training and/or strength training (89).

Figure G6.3. Exercise Interventions To Prevent Falls in Older Adults



Pooled rate ratio 0.71 (95% CI 0.61 to 0.82; *P*<0.001). Tests for heterogeneity Q = 21.49, *P*=0.044; I2 = 44%.

Source: Adapted with permission from Age and Ageing 2007;36 pp.656-62, Figure 2b. "Rethinking individual and community fall prevention strategies: a meta-regression comparing single and multifactorial interventions." Campbell A and Robertson M.

Figure G6.3. Data Points

Trial	Rate Ratio*	95% CI Lower Limit	95% CI Upper Limit	SE
Wolf et al., 1996 (a) (78)	0.525	0.321	0.86	0.138
Wolf et al., 1996 (b) (78)	1.14	0.733	1.76	0.262
Buchner et al., 1997 (89)	0.61	0.39	0.93	0.138
Campbell et al., 1997 (81)	0.68	0.52	0.90	0.097
Campbell et al., 1999 (b) (80)	0.87	0.36	2.09	0.441
Robertson et al., 2001 (84)	0.54	0.32	0.90	0.148
Barnett et al., 2003 (79)	0.60	0.36	0.99	0.161
Lord et al., 2003 (83)	0.78	0.62	0.99	0.094
Wolf et al., 2003 (88)	0.75	0.52	1.08	0.143
Campbell et al., 2005 (b) (82)	1.15	0.82	1.61	0.202
Li et al., 2005 (86)	0.45	0.30	0.70	0.102
Skelton et al., 2005 (85)	0.69	0.5	0.96	0.117
Voukelatos et al., 2007 (87)	0.65	0.47	0.89	0.107

Most of these trials and others were reviewed in a second systematic review by the same authors (90). The total number of participants in the 27 trials reviewed was 5,169. Four trials included women only and one study included only men. The majority of the studies involved independent older adults. One study included older adults living in retirement communities. A significant reduction in the number of all falls during the study was demonstrated in 6 of the 9 studies that included analysis of multiple falls. The reduction in the number of falls between intervention and controls ranged from 22% to 47.5%.

It should be noted that numerous trials have not shown a reduction in falls. Many fall prevention trials have been insufficiently powered. Numerous studies include too few subjects, have inadequate length of follow up or include subjects who are not at risk for falls. For this reason, many trials have not been successful at demonstrating an effect of physical activity on reducing falls (72;90).

Most of the interventions trials that have demonstrated a reduction in falls have included several exercise modalities: strength, balance training, exercises based on functional activities (e.g., chair stands, reaching, stair climbing), coordination activities (e.g., dance, ball games), walking outside or other endurance activities, and progression in the difficulty and complexity of the program. Currently, interventions with the most evidence include strength and balance training to reduce falls. One meta-analysis pooled and analyzed 4 trials that used a similar exercise intervention (the Otago Exercise Programme from New Zealand, which focuses on home-based strength and balance training) (76). The meta-analysis included 1,016 community dwelling women and men aged 65 to 97 years. The results from this study demonstrate a reduction in falls of 35% (95% CI 0.57 to 0.75). In addition, this analysis demonstrated a 35% reduction in the number of injurious falls (95% CI 0.53 to 0.81). Subjects aged 80 years and older benefited significantly more than did subjects aged 65 to 79 years of age.

Evidence also exists that tai chi exercise training programs provide benefit (75;77;86;87), although the evidence is inconsistent (77). Tai chi exercises consist of slow but continuous movements of all parts of the body incorporating elements of strength, balance, coordination, postural alignment, and concentration (77). All of these areas of fitness are related to risk of falls. To date, several studies examining tai chi have shown a reduction in falls in older adults (78;86;87). The reason for the success of these trials may be due to their study design in terms of size (all studies had more than 200 subjects) and duration (all studies lasted for 1 year or longer).

Pattern of Exercise

The frequency and duration of the exercise programs in the successful exercise trials vary. In the 9 positive exercise interventions (out of 13) analyzed in the recent meta-analysis by Campbell and Robertson (70), frequencies included 1 hour per week of center-based strength, balance, endurance and coordination instruction with home exercises encouraged (79), 1 hour 2 times per week of center-based strength, balance, endurance, and coordination instruction (83), 1 hour 3 times per week of center-based strength and/or aerobic training

(89), 30 minutes 3 times per week of home-based strength and balance with additional encouragement to walk for 30 minutes 2 or more times per week (81;84), 1 hour per week to 1 hour 3 times per week of tai chi (86), 45 minutes 2 times per week of center-based tai chi with daily home exercises encouraged (78), center-based strength, balance, flexibility and endurance program for 36 weeks for 1 hour a week, and the home-based Otago Exercise Programme 2 times a week for 30 minutes (85).

The falls prevention program from New Zealand — the Otago Exercise Programme — merits description, as it has been studied the most. The details of this program are outlined in an instructional review paper (91). Briefly, through several home visits, a trained instructor teaches an individualized, progressive, moderate-intensity lower body muscle strengthening exercises using ankle cuff weights in addition to balance exercises. Balance exercises progress from holding on to a stable support, such as furniture, to performing exercises independent of support. Exercises include: knee bends, backward walking, sideways walking, tandem stance and walk, heel walking, toe walking, and sit-to-stand. The participant is instructed to perform these activities 30 minutes 3 times per week and is also encouraged to walk outside for at least 30 minutes 2 or more times per week.

A few caveats of these results should be noted. First, the benefits continue as long as the programs are carried out (80) but there is no reason to believe that benefits would persist once the programs are stopped. In addition, the activities must be specifically designed for fall prevention. Less-specific exercise programs, such as brisk walking do not reduce falls. In fact, one program of brisk walking increased the fall rate (92). Also, high-intensity training in a frail population may increase musculoskeletal symptoms without decreasing falls (66). The intensity of most of the successful interventions would be considered moderate. Lower-intensity interventions do not seem to be of much value (93-95).

Sex, Age, and Race/Ethnicity

Far more women than men have participated in research studies on falls (69). However, it appears that men and women benefit equally from physical activity falls prevention programs (63;76). Although the sex of participants may not have a significant impact on success of intervention trials, age does. Exercise programs are most successful when they include subjects aged 80 years and older and/or include subjects who have a history of falling (70). This is most likely due to baseline impaired strength and balance arising from low levels of physical activity that underlie many falls experienced by elderly people, especially those aged 80 years and older. Currently, no data are available to ascertain whether response to physical activity and falls prevention differs by race or ethnicity.

Comparison to Current Guidelines

Current recommendations from the ACSM and the AHA include balance training for older adults at risk of falls as well as aerobic and strength training (68). In addition, guidelines for the prevention of falls from the American Geriatric Society also recommend physical activity, especially with balance training as one of the components (69). It should be noted that neither the ACSM/AHA nor the AGS guidelines provide recommendations for the frequency or duration of balance training.

The Otago Exercise Programme used in 4 intervention trials meets the ACSM/AHA recommendations, and this program has been shown to be successful at reducing falls in older community-dwelling people (76). Evidence also suggests that programs meeting just less than the ACSM/AHA recommendations (e.g., frequency of less than 5 days per week) also are successful at reducing falls (79;83;85). However, all of these programs still combine muscle strengthening and balance exercises in addition to walking. The results from the studies that focused on tai chi are more difficult to compare to the ACSM/AHA recommendations due to the nature of the activity, but clearly, balance is an important element of tai chi and several of the tai chi trials showed a reduction in falls (75;77;86;87).

Overall Summary and Conclusions

Regular physical activity has substantial health benefits. It is important to characterize the benefits in terms of preventing diseases and premature mortality, which is the purpose of most chapters of this report. It is also important to characterize the benefits in terms of the impact of physical activity on ability to perform the tasks of everyday life, which is the overarching purpose of this chapter. The Functional Health subcommittee focused on 3 questions pertaining to middle aged and older adults: (1) Does physical activity prevent or delay the onset of functional limitations and/or role limitations? (2) In adults with existing functional limitations and/or role limitations, does physical activity have a beneficial effect on functional ability and role ability? (3) Does physical activity reduce risk of falls and injurious falls?

Scientific evidence pertaining to each of these questions was systematically sought and reviewed. Based upon this evidence, the subcommittee’s main conclusions are:

- Strong, consistent observational evidence indicates that mid-life and older adults who participate in regular physical activity have reduced risk of moderate or severe functional limitations and role limitations. Active mid-life and older individuals — both men and women — have approximately a 30% lower risk of developing moderate or severe functional limitations or role limitations compared with inactive individuals. The evidence of benefit is strong for aerobic activity, but limited for other types of activity (muscle-strengthening, balance, and flexibility activities).

- In older adults with existing functional limitations, moderate, fairly consistent evidence indicates that regular physical activity is safe and has a beneficial effect on functional ability. The evidence of benefit is moderate for physical activity involving both aerobic and muscle strengthening activities, but evidence is limited for any single type of activity used alone. Further, evidence to conclude that physical activity improves or maintains role ability is currently limited.

- In older adults at risk for falls, evidence is strong that regular physical activity is safe and reduces falls. The evidence of benefit is strong for physical activity programs that emphasize both balance training and muscle-strengthening activity, and also include some aerobic activity, especially walking. Moderate evidence also indicates that tai chi exercise programs provide benefit, although the data are inconsistent. In older adults without substantial functional limitations and at low risk of falls, limited evidence indicates that physical activity reduces fall risk. Further, limited evidence suggests that physical activity reduces risk of injurious falls (e.g., fractures) in older adults.

In addition, previous reviews of scientific evidence have established that physical activity in middle-aged and older adults improves physical fitness and physiologic capacity (aerobic, strength, and balance) even into advanced age (3;96).

In summary, physical activity can help prevent or delay the onset of functional and/or role limitations, improve functional ability, and reduce falls. Because older adults have the lowest physical activity participation rates of any age group and have the highest risk of disability, increasing physical activity in older adults is an important public health goal.

Research Needs

It is important that future research on older adults and physical activity develop a consensus around standardized and meaningful outcomes for assessing functional health and disability. Developing universally agreed-upon outcome measures in this area will greatly assist future evaluations of research. The research to date demonstrates that moderate-intensity, multi-modal interventions appear to have benefit. However, it is not known whether: 1) single-mode interventions (e.g., walking alone) are equally effective; 2) a threshold or dose effect of physical activity exists that affects functional health; 3) higher intensity interventions are more or less effective than moderate-intensity activity and 4) these interventions are equally effective in understudied populations.

The impact of power training on improving functional ability in older adults has been addressed in a few trials and shows promise (60;97) and is addressed in greater detail in ***Part G. Section 5: Musculoskeletal Health.*** Future research should address more fully whether power training is effective, feasible, and safe for older adults with functional limitations. Most importantly, due to the high economic costs associated with disability, future research needs to focus on large-scale well-designed trials to ascertain whether physical activity programs can prevent disability and role limitations as people advance into old age.

With respect to falls, although existing research provides strong evidence that physical activity programs decrease fall risk, it is still not clear which programs are most suitable for which population groups. For example, is tai chi better for a younger population and an individualized home-based program more suitable for those who are older? Similar to

Question 2, it appears that moderate intensity multi-modal interventions appear to have benefit. However, we do not know whether there is a threshold or dose effect of physical activity on reducing falls or whether higher-intensity interventions are more or less effective. We also do not know whether interventions are equally effective in across all population groups. To date, only a few research studies have addressed whether injurious falls are reduced with physical activity programs in older adults (80). Although fractures are discussed in detail in ***Part G. Section 5: Musculoskeletal Health,*** it deserves mentioning here that an RCT with sufficient power is needed to assess whether physical activity can reduce fractures as an endpoint. This is an important research topic because 90% of hip fractures result from falls.

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Part G. Section 7: Cancer

Introduction

In the United States, an estimated 45% of men and 38% of women will develop cancer in their lifetimes (1). Only 10% to 15% of cancers are due to an inherited genetic predisposition, and the remainder is thought to be due to lifestyle or environmental factors (2). The International Agency for Research on Cancer (IARC) estimates that 25% of cancer cases worldwide are due to overweight and obesity and a sedentary lifestyle (2). The most consistent associations between increased physical activity and reduced cancer risk have been observed for colon and breast cancers. Growing evidence supports a reduced risk of endometrial and lung cancers in physically active versus sedentary persons. A large number of studies have investigated the association between physical activity and prostate cancer and, in summary, have found no association between physical activity and risk of prostate cancer. Few data are available to determine whether physical activity affects risk of cancer at other sites.

A total of 1,437,180 new cancer cases and 565,650 deaths from cancers were projected to occur in the United States in 2008, and cancer is the leading cause of death for men and women younger than age 80 (1). A growing body of literature supports a role for physical activity in improving cancer prognosis and quality of life (3). Therefore, it is imperative to identify lifestyle factors that could be modified to reduce the impact of cancer.

Review of the Science

Overview of Questions Asked

This chapter addresses 3 specific questions:

1. What are the associations between physical activity and incidence of specific cancers? If an association exists, what is the dose-response pattern?

2. What are the effects of physical activity on cancer survivors, including late and long-term effects of treatment, quality of life, and prognosis?

3. What mechanisms explain the associations between physical activity and cancers?

Data Sources and Process Used to Answer Questions

This chapter reviews the available epidemiologic data on associations between physical activity and risks of specific cancers, the intervention study data on physical activity in cancer survivors, and the human experimental data on mechanisms that might explain the links between physical activity and cancer. The Cancer subcommittee began its literature review with the *Physical Activity Guidelines for Americans* Scientific Database, which includes publications since 1995 (see ***Part F: Scientific Literature Search Methodology***, for a full description of the Database). This search was augmented with MEDLINE searches of English-language articles using the terms “physical activity,” “exercise,” and “cancer.” In addition, the subcommittee used several comprehensive literature reviews (2;4-8).

Because all of the studies that examined the association of physical activity with risk of cancer are observational epidemiologic studies, causality cannot be inferred. However, chance is unlikely as an alternate explanation because many of the results were statistically significant, particularly for colon and breast cancer.

Question 1. What Are the Associations Between Physical Activity and Incidence of Specific Cancers? If an Association Exists, What Is the Dose-Response Pattern?

Conclusions

A large body of epidemiologic data exists on the association between physical activity and the risk of developing various types of cancer. Although the direct evidence of these associations derives only from observational studies, randomized controlled trials (RCTs) have provided indirect evidence by examining the association of physical activity with markers of cancer risk, such as circulating levels of sex hormones, insulin, and cytokines.

The observational data are clearest for colon and breast cancer, with case-control and cohort studies supporting a moderate, inverse relation between physical activity and the development of these cancers. Individuals engaging in aerobic physical activity for approximately 3 to 4 hours per week at moderate or greater levels of intensity have on average a 30% reduction in colon cancer risk and a 20% to 40% lower risk of breast cancer, compared with those who are sedentary. A dose-response relation also is apparent, with risk decreasing at higher levels of physical activity. However, little information is available regarding what additional amounts and intensity of physical activity are associated with additional risk reductions; it also is unclear what the magnitude of the additional decrements in risk may be. The available evidence suggests that at least 30 to 60 minutes per day of moderate to vigorous intensity physical activity is required to significantly lower the risk of colon and breast cancer.

Compared with sedentary people, the available epidemiologic data suggest that active people have approximate reductions in risk of lung, endometrial, and ovarian cancers of

20%, 30%, and 20%, respectively. The data overall do not support associations of physical activity with prostate or rectal cancers. Too few data exist regarding the other site-specific cancers to make reasonable conclusions.

Rationale

Breast Cancer

Overall Associations

More than two dozen prospective cohort studies (9-34), and an even greater number of population-based case-control studies (35-71) have examined the relation between physical activity and breast cancer risk. These studies have primarily assessed the role of recreational physical activity on breast cancer risk. Overall, most studies suggest that physically active women have a lower risk of developing breast cancer than sedentary women. The majority of reported cohort studies (10-15;17;18;20-22;24;27;29;31-34) have reported a reduction in risk with physical activity ranging from 20% to 80%, and a number of population-based case-control studies (35-37;41-49;51;53;54;56;69-71) have reported reduction in risk ranging from 20% to 70%. In a meta-analysis of 23 studies focused on physical activity in adolescence and young adulthood, a summary relative risk (RR) estimate of breast cancer for highest versus lowest category of physical activity was 0.81 (95% CI 0.73-0.89), and each 1-hour increase of recreational physical activity per week was associated with a 3% (95% CI 0%-6%) risk reduction (72). A more extensive systematic review of recreational activity and breast cancer risk included 19 cohort and 29 case-control studies (73). The review concluded that evidence was strong that physical activity reduced risk of postmenopausal breast cancer by 20% to 80%, and that each additional hour of physical activity per week reduced risk for breast cancer by 6% (95% CI 3%-8%). They further concluded that the effect of physical activity on premenopausal breast cancer risk was a more modest 15% to 20% reduction.

The relevant lifetime periods for the effects of physical activity on breast cancer risk are not established. Lifetime recreational physical activity (35;51;54;64), adolescent physical activity (15;17;24;35;42;45;47), and physical activity at various life points (10-14;17;18;22;24;37;47;49;51;60) have been associated with lower breast cancer risk in several studies. Studies examining risk more broadly for specific decades of life also have observed an inverse association with some or all examined time periods (24;45;58;59). Furthermore, physical activity after menopause has been found to reduce breast cancer risk (12;22;24). Other studies that specifically looked at physical activity at various life periods have not found a reduced breast cancer risk with physical activity at any time (25).

Associations for Specific Subgroups

Within the United States, associations between increased physical activity and decreased breast cancer risk have been observed in multiethnic populations (24;70;71). These observations also hold true for specific racial and ethnic populations, including black (46;70), Hispanic (49;71), and Asian American women (56).

Results from some studies with sufficient numbers in subgroup populations suggest that the association with physical activity may be stronger in women without a family history of breast cancer than in those with a family history (22;34;51;69), although other large studies have found that women with as well as women without a family history of breast cancer had reduced risk of breast cancer with increasing physical activity (24;32). Several previous studies reported a greater reduction in risk with increasing physical activity among parous compared to nulliparous women (34;35). However, other studies have either observed the opposite finding with risk reduction greater in nulliparous women (32;44), or have found no effect modification of parity (24). One study found that physical activity may be more strongly associated with reduced risk of postmenopausal breast cancer in women who do not use menopausal hormones (22;71), though other studies found that physical activity effect did not change according to menopausal hormone use (16;24;32;40;64).

In 4 studies, researchers examined effect modification by adult weight gain (14;17;45;74), and 1 study reported a greater reduction in risk among women who had less than a 17% increase in adult weight (74). Several studies documented a greater reduction in risk among leaner women compared to heavier women (11;24;44;51), although other studies found that physical activity reduced risk of breast cancer in women with all levels of body mass index (BMI) (32;34).

Two cohort studies have addressed the effect of physical activity on breast cancer within the context of other variables related to energy balance, specifically adiposity and dietary energy intake. One study found evidence that premenopausal women who did not participate in vigorous activity, were overweight or obese (BMI greater than 25 kg/m^2), and had a relatively high calorie intake (more than 1,970 kilocalories per day, as determined from a food frequency questionnaire), had a statistically significant 60% increased risk of breast cancer compared with active, normal weight women with lower calorie intake (26). Another cohort study found that women with the highest quartile of energy intake, were obese, and participated in less than 4 hours per week of vigorous physical activity, had a RR of 2.1 (95% CI 1.27-3.45) compared with normal or overweight, active women who had the lowest quartile of calorie intake (31).

In hypothesizing about the reasons for the effects of energy balance on breast cancer risk, investigators speculate that, in addition to the potential role of obesity as an effect modifier, obesity possibly may be on the causal pathway between physical activity and postmenopausal breast cancer development. Specifically, physical activity reduces levels of adiposity, and subsequently reduces adipose tissue production of estrogen and testosterone, both of which can promote breast carcinogenesis or progression. However, most studies of physical activity and breast cancer have adjusted for BMI as a proxy for adiposity, and an inverse association between physical activity and breast cancer risk persisted. Thus, it is likely that physical activity may have some effect on breast cancer risk independent of their mutual relation with adiposity.

Dose-Response Pattern

Several studies have tried to quantify the level of physical activity required for a decreased risk of breast cancer. Investigators have reported statistically significantly lower rates of breast cancer among women exercising at least 1 hour per week (14); exercising at least 3.8 hours per week (primarily vigorous exercise) (35); exercising to keep fit at least 4 hours per week (11); and exercising vigorously at least 7 hours per week (46). Other investigators have observed significantly lower rates among women expending at least 1,500 kilocalories per week (18) (approximately 4 hours per week of moderate-intensity activity); at least 15.3 metabolic equivalent (MET)-hours per week (approximately 4 hours per week of moderate-intensity activity) (41); and at least 17.6 MET-hours per week (4 to 5 hours per week of moderate-intensity activity) (74). Two reports from the same study found significantly lower rates of breast cancer only among women who exercised vigorously on a daily basis during the ages to 14 to 22 years (45;68). Finally, in a study where total physical activity over the lifetime was assessed, significantly lower breast cancer rates were seen in women who expended at least 47.5 MET-hours per week per year in total activity (48). The impact of these various levels of activity on reducing risk has varied from 20% to 40%. However, other studies that specifically looked at dose-response have had not found an effect of any dose of exercise on breast cancer risk (28;30). Overall, it appears that at least 4 to 7 hours per week of moderate to vigorous intensity physical activity is required to produce a statistically significant reduction in risk, although some evidence suggests greater reduction in risk with greater amount of activity, such that 1 hour per day of moderate or vigorous activity produces greater reduction in risk compared with the Surgeon General recommendation of 30 minutes per day on most days of the week (4).

Tumor Characteristics

The incidence of *in situ* breast cancer is largely influenced by prevalence of screening, and therefore it is important to examine the effects of physical activity on invasive breast cancer separately from that on *in situ* breast cancer. Furthermore, breast cancers consist of distinct biological subtypes that are strongly related to prognosis and that may differ in etiology including tumor responsiveness to hormones (i.e., estrogen and progesterone receptor [ER/PR] status positive or negative), and other tumor characteristics (e.g., Her2neu receptor status, and other proliferative indices). A few studies have separately examined the association between physical activity and *in situ* versus invasive breast cancer, however, very few have examined physical activity effects separately in hormone receptor positive or negative tumors, and none has considered other tumor characteristics. In one study, researchers examined the association between physical activity and breast cancer stratified by stage of disease and found risk reduction to be greater for localized invasive disease compared to either *in situ* or regional/distant breast cancer (54). A recent large cohort study found a greater risk reduction for *in situ* (RR 0.69, *P* for trend 0.04) than for invasive breast cancer (RR 0.80, *P* for trend 0.02) (34). One case-control study focused specifically on in situ breast cancer, and found that risk of this stage of breast cancer was approximately 35% lower in women reporting any lifetime exercise activity compared with sedentary women (54). Two studies also reported risk ratios separately for ER/PR positive and negative tumors, but neither found a difference in risk by ER/PR subtype (18;75). A recent cohort study found that women who reported high versus low levels of physical activity at enrollment had a 13%, 33%, and 20% decreased risk of developing ER+/PR+, ER+/PR−, and ER−/PR− breast cancer, respectively (29). Another large cohort study found the greatest risk reduction from increased physical activity for ER−/PR− breast cancer (34). Most other studies have included too few women with hormone receptor negative disease to be able to assess the association of physical activity with risk of this subtype of breast cancer.

Type of Physical Activity

An association of sedentary occupations with increased risk of breast cancer has been documented in reports from some (11;17;27) but not other (76) prospective cohort studies. Published reports from some (43;47;48;53;61;77) but not other (41;44;52;55;56) population-based case-control studies also document an inverse association between occupational physical activity and breast cancer risk.

The effect of low-intensity activity (such as household activities, gardening, dancing, leisurely walking, or other activities with a MET score below 4) on breast cancer risk is still unclear, but may be of importance, particularly for postmenopausal breast cancer, as a large portion of activity among postmenopausal and elderly women is not vigorous. Although previous studies have examined the association between leisure-time physical activity, such as walking, biking, swimming, and aerobics, few studies have included the effects of other low-intensity activities, such as gardening, housework, or shopping, in their calculation of leisure-time physical activity. This may lead to an underestimation of true energy expenditure, especially among groups of women who do not have access to recreational or sports activity. In support of the importance of household activity, a recent large European cohort study found that for women in the highest versus lowest household activity quartile, risks for postmenopausal and premenopausal breast cancer were reduced by 19% (*P* for trend 0.0001) and 29% (*P* for trend 0.0003), respectively (33).

Prostate Cancer

Overall Associations

A number of epidemiologic studies have examined physical activity and prostate cancer risk (28;78-123), including 25 cohort studies (28;78;80-82;87-89;91-102;117;119-121;123) and 14 case-control studies (104-116;118). Several of the cohort studies (78;80;81;94;117) included prostate cancer mortality or advanced or metastatic prostate cancer as at least one endpoint. One study (91) also examined the association between cardiopulmonary fitness and risk of prostate cancer.

Of these studies, 19 found some suggestion for an inverse relation between physical activity and prostate cancer (80;81;87;89;91;93;94;96;97;101;102;104;105;109;112;113; 117;120;123). No overall association between physical activity and prostate cancer was found in 14 studies (28;82;88;95;98-100;106;108;110;114;115;119;121), and an increased risk of prostate cancer among physically active men was found in some studies (78;92; 107;111). The size of the association ranged from an 80% reduction in prostate cancer risk for the highest physical activity levels (113) to a 220% increased risk in one study (111).

Associations for Specific Subgroups

No consistent subgroup effects have been defined for demographic or health factors such as age, race/ethnicity, or BMI. A recent study found that, among men with a family history of prostate cancer, risk for those in the highest quartile of physical activity was reduced by 52%, compared to that for those in the lowest quartile of physical activity. Those without a family history had no risk reduction (115).

Dose-Response Pattern

Several studies have attempted to quantitate a dose-response association of prostate cancer risk with levels of physical activity (82;87;88;91-96;98;100-102;104-106;108-110; 112-118;120;121). A statistically significant trend toward decreasing prostate cancer risk with increasing physical activity level was observed in several studies (87;93;94;102;104; 105;113;118;120), although this was limited to advanced disease in two studies (120;124). In one study, a 74% reduction in prostate cancer risk was found in the highest compared to the lowest quartile of fitness level (91).

Type of Physical Activity

Occupational activity was associated with a decreased risk of prostate cancer in several studies (80;81;93;97;105;113;116) and recreational activity decreased risk of either overall or advanced prostate cancer in several additional studies (91;93;94;96;101;104;115;117). In one study, non-significant risk decreases were found for occupational and recreational activity but an increased risk was observed for household activity (115). No study differentiated between types of recreational activity, such as aerobic or resistance exercise, or to their subtypes such as jogging versus walking. Rather, activities were combined into measures of MET-hours per week, or to measures of frequency or total duration of activity per week.

Effect of Tumor Detection

One consideration for prostate cancer is the effect of screening. Prostate-specific antigen (PSA) screening for early detection became widespread in the United States in the 1990s. If physically active men also are more health conscious (i.e., they are more likely to be screened for prostate cancer), it may result in higher observed rates of prostate cancer among these men because of increased detection. This notion is supported by several cohort studies (94;117;120), which identified a reduction in risk of aggressive, metastatic, or fatal prostate cancer with increased physical activity level. In contrast, an investigation of physical activity and prostate cancer, diagnosed in 1988 or earlier (before widespread PSA screening was available), among Harvard University alumni found an almost halving of prostate cancer incidence rates among men aged 70 years or older who expended at least 4,000 kilocalories per week in physical activity, compared with those expending less than 1,000 kilocalories per week (84). However, an updated analysis of these men, examining prostate cancer diagnosed after 1988, did not support the earlier observations (100). These inconsistent findings may have been due to bias arising from increased screening for prostate cancer among the most active men.

Colon Cancer

To examine the association between physical activity and colon cancer, the Cancer subcommittee searched the *Physical Activity Guidelines for Americans* Scientific Database. Because the association of physical activity with colon and rectal cancer appears different (see rectal cancer below), we did not include studies where colorectal cancer was the outcome of interest, as the relation between physical activity and colon cancer likely would be diluted. The search yielded 23 publications eligible for inclusion in the present report.

Overall Association

The 23 publications reviewed represented 12 prospective cohort studies (28;99;124-133) and 8 case-control studies (134-140). Four of these publications (137-140) pertained to different aspects of the same case-control study. The database represented by the 23 studies was large, including a total of 9,747 cases of colon cancer with approximately equal distribution between the sexes (4,933 in men and 4,814 in women). The studies were conducted in the United States (124-126;129;131;132;137-142), Europe (Denmark (28), Finland (99;127), Italy (143), Norway (133), Sweden (128) and Switzerland (136)), and Asia (China (134), Japan (130;135), and Taiwan (144)).

Overall, the studies consistently show an inverse association between physical activity and the risk of developing colon cancer, with 9 of the 12 cohort studies and 5 of the 8 case-control studies indicating significant, inverse associations with at least one domain of physical activity (e.g., occupational versus leisure-time) and/or in one sex. Across all the studies, the median RR, comparing most with least active subjects, was 0.7. More specifically, results were similar across the cohort studies (median RR = 0.8) and the case-control studies (median RR = 0.7), as well as for men and women (median RR in both sexes = 0.7). These findings, encompassing studies published in 1995 and later in the *Physical Activity Guidelines for Americans* Scientific Database, are comparable with findings from a recent review of the literature on physical activity and colon cancer risk that also included studies published before 1995 (145). In this recent review, the median RR, comparing most with least active subjects across all studies, also was 0.7 (median RR for men, 0.7; for women, 0.6).

For the prospective cohort studies, bias due to recall of physical activity is unlikely because physical activity was assessed before the development of colon cancer. Thus, any misclassification of physical activity is likely to be random, diluting associations rather than causing spurious inverse relations. The results also do not appear to be confounded by other factors associated with colon cancer risk because many studies adjusted their findings for several factors, including BMI, smoking, alcohol, diet (e.g., energy intake, intake of calcium and folate intake of fiber, vegetables, and meat), use of aspirin, screening, menopausal status and use of menopausal hormone therapy, and family history of colon cancer. In particular, the findings appear independent of BMI, with most cohort studies (9 of 12) (28;124;125;127-130;132;133) adjusting for this factor, and continuing to observe significant inverse associations. However, fewer than half the case-control studies (3 of 8) adjusted for BMI. Finally, the inverse associations observed are supported by plausible biologic mechanisms. Thus, although the data on physical activity and risk of developing colon cancer are based on observational epidemiologic studies, the inverse associations indicated by these studies are likely to be real.

Associations for Specific Subgroups

Several studies have examined whether the association between physical activity and decreased colon cancer risk varies, depending on use of menopausal hormone therapy (125;131), various aspects of diet (125;139), or BMI (125;128;130;134;138;142). The findings have been inconsistent, with the most consistent being the suggestion that the adverse impact of high BMI on colon cancer risk may be ameliorated by higher levels of physical activity (134;138;142).

Several studies also have examined whether physical activity has a different association with colon cancers occurring at different subsites of the colon. The data have been equivocal, with some studies suggesting a larger magnitude of association for cancers occurring in the proximal colon (130;136;142), while others have reported greater associations for cancers of the distal colon (128;132). Most studies, however, have observed equivalent associations or unclear differences across proximal and distal sites of the colon (125;126;131;133;135;140;143).

Dose-Response Pattern

All but one (99) of the studies classified subjects according to at least 3 levels of physical activity, allowing investigators to assess dose-response. In the cohort studies, 7 of 11 studies with at least 3 physical activity levels reported significant, inverse trends between physical activity and colon cancer risk (124;126-128;130;132;133). For the case-control studies, 4 of 8 also observed significant, inverse trends between activity level and colon cancer risk (134;136;143;144). As discussed above, because of the many different methods used to assess and classify physical activity in these studies, it is difficult to ascertain the shape of the dose-response curve, apart from noting that a dose-response relation appears likely.

Types and Amount of Physical Activity

Most studies have assessed leisure-time and/or occupational physical activity only, with one study also assessing active commuting, in the form of walking or bicycling to work (134). Because of the different questionnaires used to assess physical activity and the different categories used to group subjects in the studies, it is difficult to integrate the findings across the studies. Further, most studies presented their findings according to overall volume of energy expended, and data are sparse on specific kinds of activity associated with decreased colon cancer risk.

However, significantly lower risks of colon cancer have been observed with leisure-time physical activity (ordered in approximately ascending doses of physical activity) of at least twice a week for at least 10 minutes' duration (142), at least 4 hours per week of moderate-to-vigorous intensity recreational activity (131), at least 20 MET-hours per week of leisure-time activity (144), more than 21 MET-hours per week of leisure-time activity (132), 7 or more hours per week of recreational activities including walking (126) a median of 35.25 MET-hours per week of overall activity (130), a median of 46.8 MET-hours per week of leisure-time activity (124), and more than 94.3 MET-hours per week of active commuting (134). Additionally, the case-control study by Slattery and colleagues suggests that physical activity needs to be vigorous in intensity (137-140) to reduce colon cancer risk. Overall, these data suggest that 30 to 60 minutes per day of moderate-to-vigorous intensity physical activity may be needed to significantly lower the risk of developing colon cancer.

Rectal Cancer

In contrast to the associations observed between physical activity and colon cancer, the data on physical activity and risk of developing rectal cancer are far more mixed. More than half of the studies have reported no significant associations (99;126;130;133;143;144;146), with the remaining studies observing significantly lower risks (or of borderline significance) with higher levels of physical activity (127;128;135;136;140). In a recent review of the literature on physical activity and rectal cancer risk, the median relative risk, comparing most with least active subjects across all studies, was 1.0, indicating little association (130).

Additional Cancer Sites

The available evidence for an association of physical activity with reduced risk of lung, endometrial, ovarian, pancreatic, and other cancers is less complete than that for breast, prostate, colon, and rectal cancers. Therefore, the following sections present a general overview.

Lung Cancer

A review of the association of physical activity and lung cancer risk was included within a recently published book chapter (145). At the time of that review, 15 cohort studies and 6 case-control studies had been published, overall indicating a median of 20% reduced risk for lung cancer in the most versus the least active subjects. This present review focused on studies published between 1996 and 2006. Results indicate a 24% median reduction of lung cancer risk for the most versus least active subjects (101;147-156). As with the prior review, the reduction of risk was more obvious with case-control (median RR over 2 studies = 0.61) (154;156) than with cohort studies (median RR over 8 studies = 0.77) (101;147-153). The inverse relation of physical activity with lung cancer risk is similar for men (0.74, 8 studies since 1996) (101;147;149-153;156) and women (0.75, 6 studies since 1996) (147-149;152;154;156).

Most of the studies on the association of physical activity and lung cancer adjust for cigarette smoking. However, even with this adjustment, the potential for residual confounding is quite high. Three studies have reported risk reductions specifically for current smokers, former smokers, or never smokers (148;150;155). The risk reduction in these studies is more similar for current and former smokers (median RR of 0.61 (148;150;155) and 0.59 (148;150), respectively) than for never smokers (median RR of 1.03 for 2 studies reporting for this subgroup) (148;155). As yet, evidence is too sparse to conclude that the reduction of lung cancer risk by physical activity is isolated to current and former smokers.

The question of whether the association of physical activity with lung cancer is due to residual confounding by smoking has been addressed in 2 ways: examining consistency of association across histologic subtypes of lung cancer and exploring the association in never smokers. Smoking is more clearly established as a risk factor for some histologic subtypes of lung cancer than others. Evidence links smoking more closely to small cell and squamous cell lung cancers than to adenocarcinoma of the lung. Therefore, one indirect approach to the question of whether the association of physical activity with reduced risk for lung cancer is due to residual confounding by smoking status is to evaluate whether the association is present for all histologic subtypes, including adenocarcinoma. Three studies to date have examined whether the association of physical activity is similar across most lung cancer histologic subtypes, as well as within sex. In men, the median relative risks for lung cancer for those who are most versus least active are 0.59, 0.96, 0.80, and 0.73 for small cell, squamous cell, adenocarcinoma, and other/nonspecified histologic types, respectively (147;149;156). In women, the median RR values for most versus least active among the same subtypes are 0.81, 0.77, 0.86, and 0.56, respectively (147;148;156). This evidence suggests that the physical activity association is present across histologic subtypes, including adenocarcinoma. Another approach to determining whether the overall association of physical activity and lung cancer is due to residual confounding by smoking is to study non-smokers. The RR (or odds radio) for non-smokers was 1.32 and 0.74 in the one cohort and one case-control study to report an association specifically for non-smokers (148;155). It also should be noted that the 39% risk reduction for most versus least active current smokers pales in comparison to the reduction of risk from quitting smoking. Smoking cessation remains the most important means to reduce lung cancer risk among smokers. That stated, it would be of interest to understand better the potential mechanisms by which physical activity may assist in marginally reducing lung cancer risk among current and former smokers. To our knowledge, no research has directly addressed this question.

Endometrial Cancer

A review of the association of physical activity and endometrial cancer risk was included within a recently published book chapter (145). At the time of that review, 4 cohort studies and 11 case control studies had been published, overall indicating a median relative risk of

0.70 for the most versus the least active subjects. An update of that review, focusing on studies published since 1996 reported a similar median RR (0.70) for the 15 most recently published studies, which included 7 cohort studies and 8 case-control studies (157-171). Of these more recent studies, 5 include relative risks that are adjusted for multiple variables but not for BMI (157-160;171). The median RR of 0.73 for these studies is similar to the results after adjustment for BMI, which was 0.70. This is important because the effect of physical activity on body weight has been hypothesized to mediate the purported association of physical activity with reduction of risk of endometrial cancer.

Another factor that should be accounted for in analyses is menopausal hormone therapy, given the potential causal link between use of unopposed estrogen therapy and increased risk of endometrial cancer. For example, the median RR from the 3 case-control studies that adjusted for menopausal hormone therapy was 0.70 (165;168;170) (no cohort studies published to date have adjusted for this factor) compared to a median RR of 0.68 for the 10 case-control and cohort studies that did **not** adjust for menopausal hormone therapy (157-164;169;171).

Overall, evidence indicates an inverse association between physical activity and incidence of endometrial cancer. Further, the lack of change in the median relative risks for studies that did versus did not adjust for BMI or menopausal hormone therapy may indicate that the association is not mediated through obesity or the generally healthy lifestyle commonly associated with exogenous hormonal exposure.

Ovarian Cancer

The association of physical activity with incidence of ovarian cancer was explored in a meta-analysis and systematic review published late in 2007 (172). This review concluded that a modest inverse association exists, with a weighted pooled RR of 0.81 (95% confidence interval was 0.72-0.92). Sensitivity analyses indicated no difference of findings when summarized studies did versus did not adjust for BMI (which may be on the causal pathway) and for exogenous hormone use (e.g., oral contraceptives).

Pancreatic Cancer

A total of 8 cohort studies (173-180) and 2 case-control studies (181;182) have examined whether physical activity may reduce incidence of pancreatic cancer. Case-control studies may be particularly biased for pancreatic cancer, given that at diagnosis most patients have advanced disease, are symptomatic, and often have recent weight loss. Four of the 10 cited case-control studies of pancreatic cancer adjusted for BMI in multivariate models. In the 5 cohort studies that did not adjust for BMI (173-177), the median relative risk for the association of physical activity with pancreatic cancer incidence was 1.21. One of the case-control studies provided an odds ratio (OR = 0.78) for men that was not adjusted for BMI (182). Both of the case-control studies provided odds ratios for women that were not adjusted for BMI; the average of these was 0.82 (181;182). In spite of this inconsistent evidence, when taken in combination with the observation of a weak positive association with BMI (177;183), it remains possible that a level of physical activity sufficient for weight control would be associated with reduced incidence of pancreatic cancer.

Other Cancers

The potential for physical activity to reduce incidence of other cancers (e.g., thyroid, kidney, bladder, and hematopoietic) also has been studied. Reviews of these cancers are not included here because the data are too sparse to allow any conclusions regarding a potential relation with physical inactivity. Readers are referred to other reviews for an overview of results from these studies (2;145).

Question 2: What Are the Effects of Physical Activity on Cancer Survivors, Including Late and Long-Term Effects of Treatment, Quality of Life, and Prognosis?

Conclusions

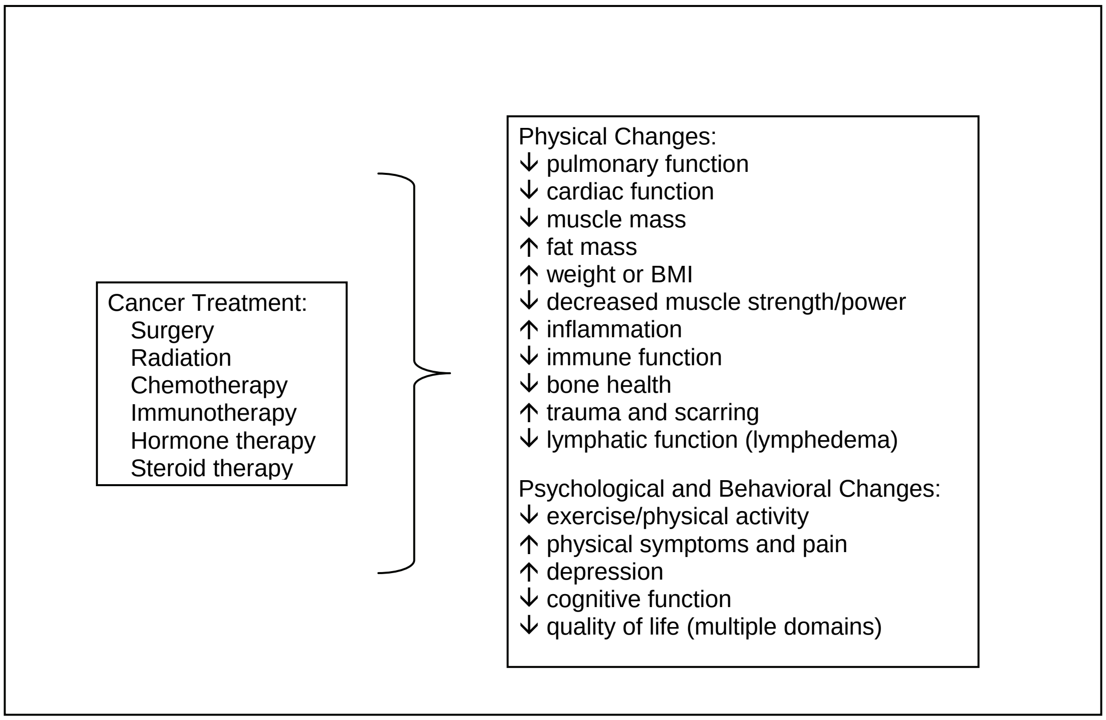
A common definition of "cancer survivor" is any individual who has had a diagnosis of cancer, from the point of diagnosis and for the balance of life. Cancer survivors are a subset of the US adult population that is expected to grow substantively in the coming decades. As such, the role of physical activity in improving outcomes for cancer survivors is likely to increase in importance as well. Recently, data have been published regarding the effects of physical activity on health outcomes among persons who already have cancer. These studies suggest that physically active individuals with breast or colon cancer may have improved prognosis (i.e., fewer recurrences and deaths), compared with sedentary survivors. In addition, physical activity may play an important role in preventing, attenuating, or rehabilitating late and long-term effects of cancer treatment. Walking is a commonly prescribed form of exercise in the studies reviewed here and appears to have benefits on muscular strength and endurance, as well as quality of life. Dose-response effects and long-term outcomes are unknown for any outcomes from physical activity interventions in cancer survivors at this time.

Introduction

More than 10 million people in the United States are cancer survivors, and more than 16% of adults older than age 65 years are cancer survivors (184). The increasing success of cancer treatments has required a shift in focus toward new outcomes, such as preventing recurrence and mortality, and accommodating the unique medical and psychosocial needs of cancer survivors.

Cancer treatment typically includes some combination of surgery, radiation therapy, or chemotherapy, and may also include hormonal therapies, steroid treatment, immunotherapies, or monoclonal antibody treatment. Each of these therapies is associated with acute as well as late and long-term adverse physiologic and psychological effects. The terms "late effects" or "long-term effects" (185) are distinct in the timing of their onset. Late effects are side effects or complications that are absent or subclinical at the end of therapy but that emerge after compensatory systems fail or some second insult (e.g., deconditioning) occurs that results in a clinically significant diagnosis that can be traced back to effects of treatment. An example of a late effect would be the diagnosis of a cardiac arrhythmia years after treatment with a cardiotoxic chemotherapeutic agent such as adriamyacin (186). Long-term effects are adverse effects or complications that appear during treatment and persist long afterward, for months, years, or the duration of life. Physical activity could be useful for preventing or attenuating some late and long-term effects of cancer treatments (Figure G7-1) (187), and may also be useful for prevention of recurrence or cancer mortality among cancer survivors.

Figure G7.1. Late and Long-Term Effects of Cancer Treatment That May Be Positively Affected by Physical Activity



The acute effects of treatment and the potential for positive effects of physical activity during active cancer treatment are beyond the scope of this review, but have been reviewed elsewhere (188;189). Also not reviewed here are the late or long-term effects of childhood cancer treatment, as little research has been conducted in this area.

Rationale

Effects of Physical Activity on Cancer Recurrence and Mortality

Though few studies have been conducted on the role of physical activity in preventing cancer recurrence or reducing mortality, the consistent findings of a preventive effect warrants comment. Data from the Nurses' Health Study were used to explore the dose-response association of physical activity with overall and breast cancer specific mortality, as well as recurrence, among 2,987 breast cancer survivors over a median of 96 months of follow-up (190). The results indicated a 29% decrease in overall mortality among women who did at least 3 MET-hours per week of aerobic activity after diagnosis, with minimal additional protection from greater levels of physical activity. The decrease in breast cancer-specific mortality and recurrence were 50% and 43%, respectively, in women who engaged in at least 9 MET-hours per week of physical activity compared with women who did less than 3. Additional benefits were small for activity levels greater than 9 MET-hours per week, which can be translated to 3 hours per week of walking at 2.5 miles per hour. Considerable evidence indicates that overweight, obesity, and weight gain are associated with breast cancer recurrence (191-193). These results are consistent with the hypothesis that physical activity reduces risk of mortality or recurrence among breast cancer survivors through weight control.

Evidence for a role of physical activity in colon and colorectal cancer survivorship comes from 2 recently published observational studies. One of these, the Nurses' Health Study, observed an inverse dose-response association of physical activity and overall and colorectal cancer-specific mortality in 554 women who had had a previous diagnosis of colorectal cancer. Women who engaged in at least 18 MET-hours per week of physical activity after diagnosis had a 61% and 57% reduced risk of colorectal cancer-specific and overall mortality, respectively, compared to women who did less than 3 MET-hours per week (194). A dose-response association of physical activity and colon cancer disease-free survival also was seen in the cohort of 832 male and female patients who participated in the CALBG trial (195). In this latter cohort, 18 MET-hours per week, or 6 hours of walking per week at 2.5 miles per hour, was associated with a 49% reduction in risk of recurrence (195).

Effects of Exercise on Prevention of Long-Term or Late Effects of Cancer Treatment

A number of recent systematic reviews (188;196-205) as well as 2 meta-analyses (188;206) have recently been conducted on the effects of physical activity interventions on a variety of outcomes in cancer survivors. Readers interested in an in-depth discussion of the effects of exercise on cancer survivors are guided to these reviews. Below, the effects of exercise training on late or long-term effects is reviewed for outcomes for which there is the greatest amount of evidence and consensus and that may be most useful in guiding quantitative or qualitative behavioral recommendations for cancer survivors. Of the 22 controlled clinical trials published since 1995 and reviewed here, only 1 (207), examined a dose-response pattern of exercise training on any outcome, and none was noted. For each of the outcomes reviewed below, effects of walking programs are noted, if such data were available. Most of the studies reviewed were relatively short in duration (6 months or less); long-term effects are not yet known.

Physiologic Effects

Cardiorespiratory Fitness. Though the effect of physical activity on cardiorespiratory fitness has been long established (see ***Part G. Section 2: Cardiorespiratory Health*** for a detailed discussion of this topic), it is of particular relevance for cancer survivors given the cardiotoxic effects of several commonly used cancer treatment drugs and radiation to the chest (186;208). A meta-analysis published in 2005 indicated a strong weighted mean effect size of 0.65 (P=0.003) for cardiorespiratory fitness based on the 4 exercise interventions that had assessed this outcome in cancer survivors after treatment (188). Since this meta-analysis, 9 additional RCTs have assessed whether various of exercise interventions in cancer survivors improve cardiorespiratory fitness after treatment (209-217). All 13 studies have shown positive effects, and 11 showed statistically significant improvements on cardiorespiratory function tests ranging from a 6-minute walk test to maximal treadmill or cycle ergometer tests. All of these studies included breast cancer survivors, and most included only breast cancer survivors. Fitness improvements have been demonstrated in a variety of programs, including walking, yoga, tai chi chuan, exercise at home, and exercise at fitness facilities. For most of the studies, exercise doses used were 3 weekly sessions of 20 to 40 minutes in duration at moderate intensity.

Muscular Strength and Endurance. Observational evidence in small convenience-sample studies suggests that muscle mass may decrease and fat mass may increase after some breast cancer chemotherapy regimens (218). Cancer treatment may result in a decrease in activity (219), with subsequent deconditioning associated with muscle disuse. Therefore, it is important to determine whether exercise training improves muscular strength or endurance in cancer survivors. Six studies have examined the effects of some form of resistance training, tai chi chuan, or yoga on muscle strength or endurance (211-213;215;220;221). All of these studies were conducted in women who had completed breast cancer treatment. Five observed positive effects of training (211;213;215;220;221) and 4 reported statistically significant improvements (211;213;215;220) in strength or endurance tests.

Flexibility. Cancer surgeries may result in decreased range of motion with scarring or tissue trauma, and these changes may result in altered physical function. Six studies have examined the effects of exercise training on flexibility. Three assessed effects of aerobic exercise or yoga on lower body flexibility with the sit-and-reach test in breast and colon cancer survivors (207;215;222). All 3 showed improvements in flexibility, but only one (207) observed a statistically significant improvement comparing changes between treatment and control participants. Three other studies examined effects of tai chi chuan, dance and movement, or aerobic exercise and stretching on shoulder range of motion in breast cancer survivors (211;223;224). All 3 noted improvements, and 2 noted significant between-group differences in shoulder range of motion (211;223).

Lymphedema. Surgical removal or irradiation of lymph nodes results in damage to the lymphatic system that can result in an inability of the affected body part to manage fluid balance and temperature regulation. This damage may impair immune response and wound healing, as well as response to trauma or injury. Swelling and pain in the affected body part can develop immediately after surgery and/or radiation or years later, making lymphedema a long-term risk among several types of survivors, including those with breast, head and neck, melanoma, genital cancers, lower gastrointestinal tract and bladder cancers. Lymphedema is considered a chronic condition, and occurs in 6% to 50% of breast cancer survivors, depending on number of nodes removed and intensity of radiation (225-227). Lower-limb lymphedema also occurs in 20% to 30% of cancer patients who have had lymph node removal or radiation in the groin or retroperitoneal lymph nodes (228-237). Four studies have examined the risk of lymphedema onset or worsening among breast cancer survivors by measuring changes in arm circumferences or symptoms resulting from exercise training (217;221;224;238). None of these studies has noted negative effects of aerobic or resistance exercise on arm circumferences or symptoms; evidence of possible benefit to the affected limb has not been examined. No studies of the safety or efficacy of exercise for cancer survivors with or at risk for lymphedema for cancer sites other than breast have been conducted.

Weight Change. Some breast cancer patients gain weight after diagnosis, and the associated changes in body composition may include decreased muscle mass and increased body fat, as suggested by a few convenience-sample studies (218). These effects have not been examined in population-based or clinical trial series of patients, nor in patients with other cancers. However, it is important to determine the effects of exercise training on body weight and body composition in survivors who have had any type of cancer treatment. The results of the 13 identified controlled trials conducted since 1995 indicate that, as for the general population, exercise may decrease percent body fat to a small degree, but has little to no effect on body weight in the absence of concurrent caloric restriction (188;207;210-215;217;222;239-241). (See ***Part G. Section 4: Energy Balance,*** for a detailed discussion of the association between physical activity, weight loss, and changes in body composition.)

Psychosocial and Symptom Effects

Quality of Life. The effect of exercise on health-related quality of life was examined in a systematic review and meta-analysis published in 2005 (188). This review concluded that evidence was strong for a positive effect of physical activity on quality of life in cancer survivors, though the weighted mean effect size of 0.30 was not statistically significant. Since the publication of that meta-analysis, an additional 10 studies have examined effects of physical activity on cancer survivors after treatment (209;213-217;223;224;240;242). Of these, all showed positive effects, and 8 indicated a statistically significant improvement in at least one quality of life indicator after a physical activity intervention. Overall, 10 out of 13 identified studies showed statistically significant improvements in quality of life resulting from a physical activity intervention after cancer treatment.

Fatigue. Cancer-related fatigue is distinct from ordinary types of fatigue in its persistence and severity (243). The effects of physical activity interventions on fatigue in cancer survivors (primarily breast cancer) have been tested in 8 studies since 1995. Of these 8 trials (207;209;210;214;216;222;239;244), 3 reported statistically significant improvements in fatigue after a program of aerobic exercise, walking, or cycling. Five other studies, most of which focused on walking programs among breast cancer survivors during the time period after treatment, observed improvements, but not statistically significant improvements. The mechanisms through which physical activity may improve cancer-related fatigue are not yet fully understood (243).

Question 3: What Mechanisms Explain the Associations Between Physical Activity and Cancer?

Conclusions

A number of plausible mechanisms might explain the associations between physical activity and cancer risk and prognosis. Increased physical activity reduces adiposity, which may explain reductions in cancers that are associated with overweight and obesity, including postmenopausal breast, colon, endometrial, and other cancers. Increased physical activity is associated with reduced levels of sex hormones, which may explain a link between physical activity and hormone-related cancers such as breast and endometrial cancers. Another possible mechanism is through the effect of physical activity and inflammation and immune function. Finally, increased physical activity reduces insulin resistance, which could explain associations with risk for some cancers, such as colon cancer, that may be increased in individuals with insulin resistance or hyperinsulinemia.

Rationale

Physical activity could affect cancer risk or progression through several plausible mechanisms (245). Many of these mechanisms may act through the effects of physical activity on obesity, with resulting changes to circulating levels of adipokines, cytokines, insulin, and sex hormones. Other mechanisms may involve direct effects on target organs and tissues. The effects of physical activity on carcinogenesis or prognosis are likely to be multi-factorial and may be affected by many factors such as age, sex, and adiposity, in addition to physical activity specific factors such as type, duration, frequency, and intensity of physical activity.

Menstrual Factors and Sex Steroid Hormones

Several modifiable menstrual factors increase breast cancer risk, including early age at menarche, frequent ovulation, regular cycles, and late age at menopause (246). Women with elevated levels of estrogens and androgens have increased risk of developing breast cancer. In a combined analysis of 9 large cohort studies, postmenopausal women in the top quintile for various estrogens or androgens had approximately double the risk of developing breast cancer compared with women in the lowest quintile (247). Elevated levels of estradiol or testosterone in premenopausal women increase risk of breast cancer as well (248;249). Medications that block estrogen receptors or that prevent estrogen production in peripheral tissues have been a mainstay of treatment for women with estrogen receptor positive breast cancer (250). Women with elevated estrogen concentrations (unopposed by progesterone) are at an increased risk for endometrial cancer (251). In men, anti-androgen therapy improves prostate cancer survival (252) and reduces overall incidence of the disease when tested as a preventive agent (253). However, recent evidence suggests that blood levels of androgens or estrogens are not related to prostate cancer risk (247), suggesting that only prostatic levels of sex hormones are relevant for prostate carcinogenesis or progression.

Premenopausal Women

The effect of physical activity on age at menarche, menstrual cycle function, and level of ovarian-produced sex steroid hormone levels in girls and young women are potential mechanisms for reduced breast cancer risk (254). Moderate-intensity physical activity may cause small changes in reproductive hormones in premenopausal women, but high intensity or volume of exercise sufficient to cause a negative energy balance may be required to induce menstrual dysfunction (amenorrhea, anovular cycles and luteal phase deficiency) with significantly decreased production of ovarian estradiol and progesterone (255-263).

Postmenopausal Women

In postmenopausal women, increased physical activity has been associated with decreased serum concentrations of estradiol, estrone, and androgens (264-266). The positive effect of physical activity is closely linked to body composition because the primary source of estrogen in postmenopausal women is from aromatization of androgen precursors in peripheral, mainly adipose, tissue. In a sub-sample from the Women's Health Initiative (WHI) Dietary Modification Trial, women with low self-reported physical activity had higher levels of estrone, estradiol, and free estradiol, and lower levels of sex-hormone binding globulin (which binds estradiol, making less available to target tissue) than did active women (265). The highest levels of estrogen were observed in women who were both below the median level for physical activity (i.e., less than 6.5 MET-hours per week, approximately less than 1.5 hours per week of brisk walking) and above the median BMI (i.e., at least 29 kg/m^2).

In an RCT, 173 overweight, sedentary postmenopausal women were assigned to a moderate-intensity aerobic exercise, 45 minutes per day, 5 days per week for 12 months or to a control group. A significant decrease in estradiol, estrone, and free estradiol was seen from baseline to 3 months in exercisers versus controls, with an attenuation of the effect at 12 months (267). However, in those women who lost body fat, the exercise intervention resulted in a statistically significant reduction in these estrogens at both 3 and 12 months. Similarly, in women who lost body fat, a statistically significant decrease in testosterone and free testosterone occurred in exercisers compared with controls (268). These intervention and observational studies results suggest that both increased physical activity and reduced body fat will produce the greatest protection against breast cancer by producing the greatest decrease in serum sex hormones.

Men

Chronically lowered testosterone concentrations have been reported in athletes, but this finding may require a threshold amount or intensity of physical activity to occur (269), and the effects of moderate-intensity aerobic exercise on sex steroid hormones in men is not known. In a recent trial, 102 men aged 40 to 75 years were randomly assigned to a 12-month moderate to vigorous intensity aerobic exercise intervention (60 minutes per day, 6 days per week) or a control group (no change in activity) (270). Dihydrotestosterone (DHT) increased 14.5% in exercisers compared to 1.7% in controls at 3 months (P=0.04). At 12 months, DHT remained 8.6% above baseline in exercisers versus a 3.1% decrease in controls (P=0.03). Sex hormone binding globulin increased 14.3% in exercisers versus 5.7% in controls at 3 months (P=0.04), while at 12 months it remained 8.9% above baseline in exercisers compared to 4.0% in controls (P=0.13). No statistically significant differences were observed for testosterone, free testosterone, 3α-Diol-G, estradiol, or free estradiol in exercisers versus controls. Therefore, the association of physical activity with circulating hormone levels in men is still unclear.

Metabolic and Other Hormones

Insulin resistance has been linked to increased risk of breast, colon, pancreas, endometrial and stomach cancers (271). Higher cancer incidence and mortality also have been noted in those with type 2 diabetes or impaired glucose tolerance (271;272). Insulin can enhance tumor development by stimulating cell proliferation or inhibiting apoptosis (271). It also can regulate the synthesis and biological availability of sex steroid hormones, and inhibit hepatic synthesis of sex hormone binding globulin (271). Acute bouts of physical activity improve insulin sensitivity and increase glucose uptake by skeletal muscle for up to 12 hours (273), and chronic exercise training results in prolonged improvements in insulin sensitivity (274-276). Although body composition has been strongly associated with insulin sensitivity, exercise-induced changes in insulin sensitivity can occur from physical activity, independent of the changes in weight or body composition (273;274;277). An additive effect of resistance training to improve insulin sensitivity and glycemic control also has been proposed because skeletal muscle is a primary site of insulin resistance (273;278).

Women with elevated levels of prolactin are at increased risk of breast cancer (279), and a recent clinical trial found that increased physical activity levels as measured by increased VO_{2max} over 1 year in a moderate-intensity exercise intervention was associated with statistically significant reductions in prolactin levels in postmenopausal, overweight women (280).

Inflammation

Elevated levels of pro-inflammatory factors, such as C-reactive protein (CRP), interleukin (IL)-6, tumor-necrosis factor-α (TNF-α), and decreased levels of anti-inflammatory factors, such as adiponectin, have been linked with increased cancer risk (281). Physical activity may reduce systemic inflammation alone or in combination with body weight or composition through reducing macrophage or adipose cell production of inflammatory cytokines in adipose tissue, although exact mechanisms are unknown (278;282).

Although cross-sectional studies support an association between chronic physical activity and lower levels of the inflammatory markers CRP, serum amyloid A (SAA), IL-6 and

TNF-α in both men and women, intervention studies of exercise alone or exercise and diet combined have had inconsistent results, with some studies but not others showing reductions in these inflammatory markers (282).

Increases in adiponectin have been seen with physical activity interventions in the presence of significant weight loss (283). Shorter duration prospective physical activity and weight loss interventions have failed to alter adiponectin levels despite modest changes in body weight and body composition (278).

Immune Function

The immune system is thought to play a role in reducing cancer risk by recognizing and eliminating abnormal cells or through acquired and/or innate immune system components (284). The role of physical activity on immune factors related to cancer has been largely untested, but one hypothesis is that physical activity could improve the number or function of natural killer cells, which play a role in tumor suppression (282).

Bouts of physical activity have been shown to result in acute increases in a number of components of immune function (e.g., neutrophils, monocytes, eosinophils, and lymphocytes), followed by a dip below pre-exercise levels lasting up to 1 to 3 hours (285). For chronic physical activity, an inverted J-shaped dose-response relation between intensity of physical activity and immune function has been shown. Moderate physical activity results in enhanced immune function, but exhaustive exercise, overtraining, or high-intensity exercise may lead to immunosuppression, which may result in increased susceptibility to ailments such as upper respiratory infections (282). However, the current evidence on moderate-intensity physical activity from randomized controlled trials is inconclusive, with differences in components of the innate immune system noted in some, but not all, cross sectional studies that compare exercisers to non-exercisers. Randomized controlled trials of moderate physical activity show little effect on immune function (282).

Other Mechanisms

Physical activity also could mediate cancer risk through additional mechanisms, such as its effects on other body structures. For example, physical activity affects colon motility, leading to decreased transit time and, perhaps, reduced carcinogen exposure in the colon (254). In addition, physical activity has been hypothesized to affect various tissues leading to reduced carcinogenic prostaglandin (PG) production (286), although an RCT found no effect of a 12-month aerobic exercise intervention (1 hour per day, 6 day per week) on colon mucosal prostaglandins PGE2 or PGF2alpha in 202 men or women aged 40 to 75 years (287).

Overall Summary and Conclusions

Increased physical activity is associated with reduced risk of several cancers. Most evidence for this association is available for breast and colon cancers, although growing evidence suggests an association between increased physical activity and reduced risk of endometrial and lung cancers. Overall, data suggest that 30 to 60 minutes per day of moderate-to-vigorous intensity physical activity may be needed to significantly lower the risk of developing breast and colon cancers. The effect of physical activity is larger for colon cancer (median reduction in risk of 30% across reviewed studies) compared with breast cancer (median reduction in risk of 20% across studies). A large part of the effect of physical activity on cancer is likely mediated through obesity and other hormonal and metabolic mechanisms. Randomized controlled trials have demonstrated effects of physical activity interventions on cancer risk factors, which further support a role of physical activity in reducing risk for cancer.

Strong evidence links increased physical activity in cancer survivors with improved quality of life and increased fitness. Less evidence is available regarding the effect of physical activity on cancer recurrence and survival. A 2006 publication from the American Cancer Society (3) states that although the current public health guidelines of 30 to 60 minutes of moderate-intensity aerobic exercise 5 times per week have not been studied systematically in cancer survivors, there is no reason to think that this would not also benefit survivors. Overall, results indicate that guidelines for cardiovascular exercise for cancer survivors who have completed treatment need not be different from those of the general population, and that particular physiologic and psychosocial effects of cancer and its treatments are positively affected by cardiovascular exercise, resistance training, and flexibility training.

Research Needs

Knowledge about the role of physical activity in reducing the risk of common cancers would benefit from additional evidence gathered from clinical trials. In the survivorship setting, clinical trials showing a benefit of physical activity interventions on reducing deaths, recurrences, and reducing the impact of late or long-term treatment effects, also would make a valuable contribution to our understanding of the needs of this growing population.

Other research needs include studies to clarify biological mechanisms linking physical activity to specific cancers in order to identify associations with less commonly studied cancers, define the shape of dose-response curve of the physical activity-cancer relation, determine the effect of low-intensity activities and accumulated bouts, and assess the effect of physical activity within specific population subgroups.

Additional observational epidemiologic research to identify the dose, type, and frequency of physical activity on risk of various cancer sites and subtypes is needed, in addition to identifying the effect of physical activity on risk of specific cancers within particular population subgroups including various race/ethnic, age, sex, and groups at elevated risk of cancer.

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Part G. Section 8: Mental Health

Introduction

Poor mental health, including diseases of the central nervous system (CNS), reduces the quality of life and adds a burden on public health. People with anxiety or depression disorders are more likely to have chronic physical conditions (1), and depression and dementia were among the 10 leading risk factors of disability-adjusted life expectancy in high-income nations worldwide during 2001 (2). They are projected to rank first and third by the year 2030 (3). In the United States, dementia and other CNS disorders are a leading cause of death, and mental disorders are estimated to account for more than 40% of years lost to disability (4).

The scientific evidence from prospective cohort studies and randomized controlled trials (RCTs) supports the overall conclusion that regular participation in moderate-to-vigorous physical activity is associated with improved aspects of mental well-being and reduced symptoms of several mental health disorders.

Review of the Science

Overview of Questions Asked

This chapter addresses 7 general questions about physical activity and mental health conditions. Each question includes subsections that focus on whether physical activity can protect against the onset of, or reduce, symptoms; whether the effects of physical activity on the symptoms differ by age, sex, race/ethnicity, or medical condition; and whether the effects of physical activity differ by the type, intensity, or timing of the physical activity. The general questions are:

1. Is there an association between physical activity and depression?
2. Is there an association between physical activity and anxiety?
3. Is there an association between physical activity and distress and well-being?
4. Is there an association between physical activity and cognitive function and dementia?
5. Is there an association between physical activity and sleep?

6. Is there an association between physical activity and other aspects of mental health?

7. Is there an association between physical activity and adverse psychological events?

The chapter also considers a final question dealing with mechanisms that could plausibly explain the association between physical activity and mental health.

Data Sources and Process Used to Answer Questions

To provide evidence-based answers to the above questions, the Mental Health subcommittee obtained data from a search of the *Physical Activity Guidelines for Americans* Scientific Database (see ***Part F: Scientific Literature Search Methodology,*** for a full description of the Database), which contains studies published in 1995 and later. Conclusions regarding the evidence-based review were restricted to results of RCTs and observational studies that used a prospective cohort design. Findings from selected cross-sectional, observational studies are presented when they provided additional information for questions that had a limited number of RCTs and prospective cohort studies (e.g., anxiety disorders and sleep). Studies of physical activity and mental health published since 1995 were evaluated using meta-analytic or otherwise systematic reviews when they were available. When such reviews were not available or were not sufficiently current, a systematic quantitative synthesis of results from published studies was conducted using a random effects model that weights results by the size of each study and variation in the effects across studies. Odds ratios in observational studies and standardized effect sizes in RCTs were retrieved from the published papers, or they were otherwise estimated from data and test statistics reported in the papers (5).

Question 1: Is There an Association Between Physical Activity and Depression?

Introduction

The American Psychiatric Association (6) recognizes 4 types of mood disorders: (1) *depression*, (2) *bipolar or manic-depressive disorder*, (3) mood disorders due to a *medical condition*, and (4) *substance-induced* mood disorders. Depression has an annual prevalence of about 8% among women and 4% among men worldwide and in the United States. The annual cost of depression in the United States is estimated at $83 billion per year (7). This condition includes a mild chronic form, *dysthymia*, and a more severe form, *major depressive disorder*. The rate of major depression has increased steadily during the past 50 years, with a lifetime prevalence of about 16%; the rate is higher among Hispanics than whites, and lowest, though still substantial, among African Americans. The lifetime rate of depression among adults aged 30 to 60 years is about twice the rate among people older than age 60 years (8).

People have a major depressive episode when they have depressed mood or lose interest or pleasure in normal activities most of the time for at least 2 weeks. Other symptoms include abnormalities in appetite, libido, sleep, energy levels, concentration and, often, suicidal thoughts. In some cases, anxiety and motor agitation can be more prominent symptoms than depressed mood. Also, mood disturbance can be less apparent than other features such as irritability, abuse of alcohol, and worsening of comorbid phobias, obsessions, or preoccupation with physical symptoms. Depression is not considered a major depressive episode if it is caused by grief (less than 2 months), drug abuse or medication, or a medical condition such as hyperthyroidism, heart disease, diabetes, multiple sclerosis, hepatitis, or rheumatoid arthritis. Many older patients with symptoms of depression do not meet the full criteria for major depressive disorder. If they have similar, but fewer, symptoms they may have *minor depression*, a sub-syndromal form of depression.

Does Physical Activity Protect Against the Onset of Depression Disorders or Depression Symptoms?

Conclusions

Population-based, prospective cohort studies provide substantial evidence that regular physical activity protects against the onset of depression symptoms and major depressive disorder. Evidence is insufficient to draw conclusions about bipolar disorder and other mood disorders.

Rationale

An association between physical activity and reduced symptoms of depression among adults has been generally supported in more than 100 population-based observational studies published since 1995, including nationally representative samples of nearly 190,000 Americans (9-15). Most of the studies looked at cross-sectional associations, which indicated that active people on average had nearly 45% lower odds of depression symptoms than did inactive people. In the national samples of Americans, active people had approximately 30% lower odds of depression.

Twenty-eight of the studies used a prospective cohort design, which reduces the likelihood that the association is explainable by people becoming less active after they experience depression symptoms. The median follow-up was about 4 years, and the range was 9 months to 37 years. The studies came from 11 nations (Australia, Canada, China, England, Finland, Germany, Israel, Italy, Netherlands, Japan), including 13 studies from the United States. In the cohort studies, the average odds of elevated symptoms were about 25 to 40% lower among active compared with inactive people, without adjustments for depression risk factors that might have differed between the active and inactive groups (OR = 0.67, 95% CI = 0.59 to 0.77). After adjustment for risk factors, such as age, sex, race, education, income, smoking, alcohol use, chronic health conditions, and other social and psychological variables, the odds remained nearly 15 to 25 percent lower among active people (OR = 0.82, 95% CI = 0.78 to 0.86).

Nearly all the comparisons (66 of 67) in the cohort studies showed less depression among physically active than inactive adults, but half the results did not reach statistical significance, often because the sample sizes were not big enough. The average number of people for each comparison was about 1,100 people, but a fourth of the comparisons included 500 people or fewer. Studies of 8 cohorts (16-23) used a clinical diagnosis to measure depression symptoms, reporting a reduction in the odds of incident cases of depression that averaged 30 percent (OR = 0.71, 95% CI: 0.61 to 0.77) among active people compared to inactive or low active people. In those studies, 18 of 19 comparisons favored active people, and nearly half the comparisons were statistically significant. Thus, the protective effect of physical activity is not limited to self-rated symptoms measured by questionnaires. Figures G8.1a and G8.1b illustrate crude and adjusted odds ratios and 95% confidence intervals from the 28 prospective cohort studies of physical activity and depression in nearly 40,000 adults from 11 countries, including 11 studies from the United States.

Does Physical Activity Reduce Symptoms of Depression?

Conclusions

The results of RCTs indicate that participation in physical activity programs reduces depression symptoms in people diagnosed as depressed, healthy adults, and medical patients without psychiatric disorders.

Rationale: Depressed Patients

A meta-analysis of 14 RCTs of chronic exercise among people diagnosed with depression (24) reported a cumulative, mean reduction in depression symptoms of 1.1 SD (95% CI: 1.5 to 0.60). However, the studies had scientific weaknesses that made it hard to conclude that the reduced depression symptoms were the independent result of exercise, and only 2 of the studies had been published after 1995 (25;26). Since that review, at least 11 RCTs have used exercise training to reduce depression symptoms in about 500 depressed patients. In 3 studies (27-29), depression was identified using cut-point scores on symptom questionnaires that have good predictive validity as screening tests to detect depression. In another 8 studies (30-37), patients were identified by diagnostic interview as having major depressive disorder, minor depression, or dysthymia.

In the studies published since the Lawlor & Hopker review (24), the average effect of exercise for symptom reduction was 1.1 SD (95% CI: 1.55 to 0.64) compared to a no treatment control group, virtually identical to the Lawlor & Hopker results. These recent studies compared the effects of exercise to a placebo (29;32-34;36;38) or to drug therapy (30;38) or bright light therapy (35). The reductions, on average, favored exercise over placebo (0.35 SD, 95% CI: 0.49 to 0.22), and 6 of 14 comparisons were statistically significant. The average sample size was 58 people, but 25% of the studies had 25 people or fewer. Symptom reduction after exercise was similar to drug therapy and similar or superior to bright light therapy. Four of the studies reported that reductions in symptoms met criteria

Figure G8.1a Depression Symptoms: Prospective Cohort Studies, 1995 Through 2007: Crude Odds

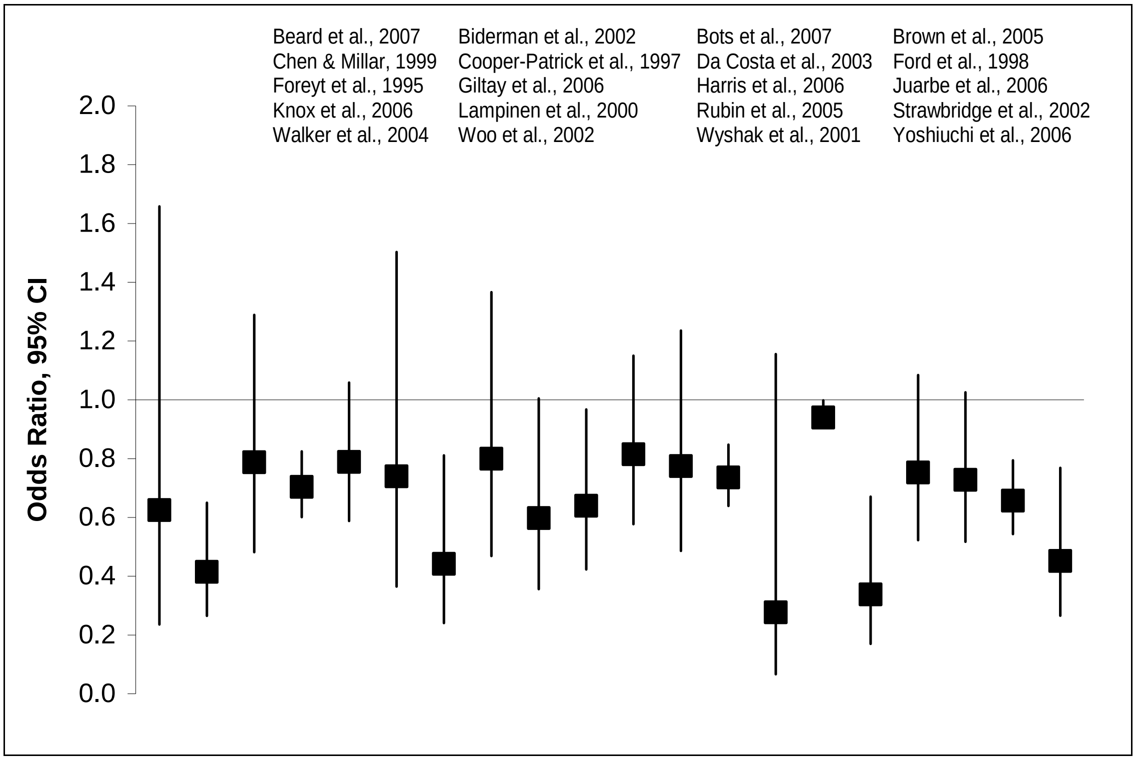

Figure G8.1a Data Points

Author/Date	High	Low	Odds Ratio
Beard et al., 2007	1.658	0.236	0.625
Biderman et al., 2002	0.6504	0.265	0.415
Bots et al., 2007	1.289	0.4819	0.788
Brown et al., 2005	0.8251	0.6011	0.704
Chen & Millar, 1999	1.0587	0.588	0.789
Cooper-Patrick et al., 1997	1.5026	0.365	0.74
Da Costa et al., 2003	0.8115	0.2407	0.442
Ford et al., 1998	1.3663	0.4686	0.8
Foreyt et al., 1995	1.0047	0.3562	0.598
Giltay et al., 2006	0.9678	0.4232	0.64
Harris et al., 2006	1.1502	0.577	0.815
Juarbe et al., 2006	1.2356	0.4861	0.775
Knox et al., 2006	0.848	0.6394	0.736
Lampinen et al., 2000	1.1555	0.0666	0.277
Rubin et al., 2005	0.9982	0.9229	0.94
Strawbridge et al., 2002	0.6709	0.1698	0.338
Walker et al., 2004	1.0842	0.523	0.753
Woo et al., 2002	1.0253	0.5173	0.728
Wyshak et al., 2001	0.7946	0.5432	0.657
Yoshiuchi et al., 2006	0.7689	0.2658	0.452

Figure G8.1b Depression Symptoms: Prospective Cohort Studies, 1995 Through 2007: Adjusted Odds

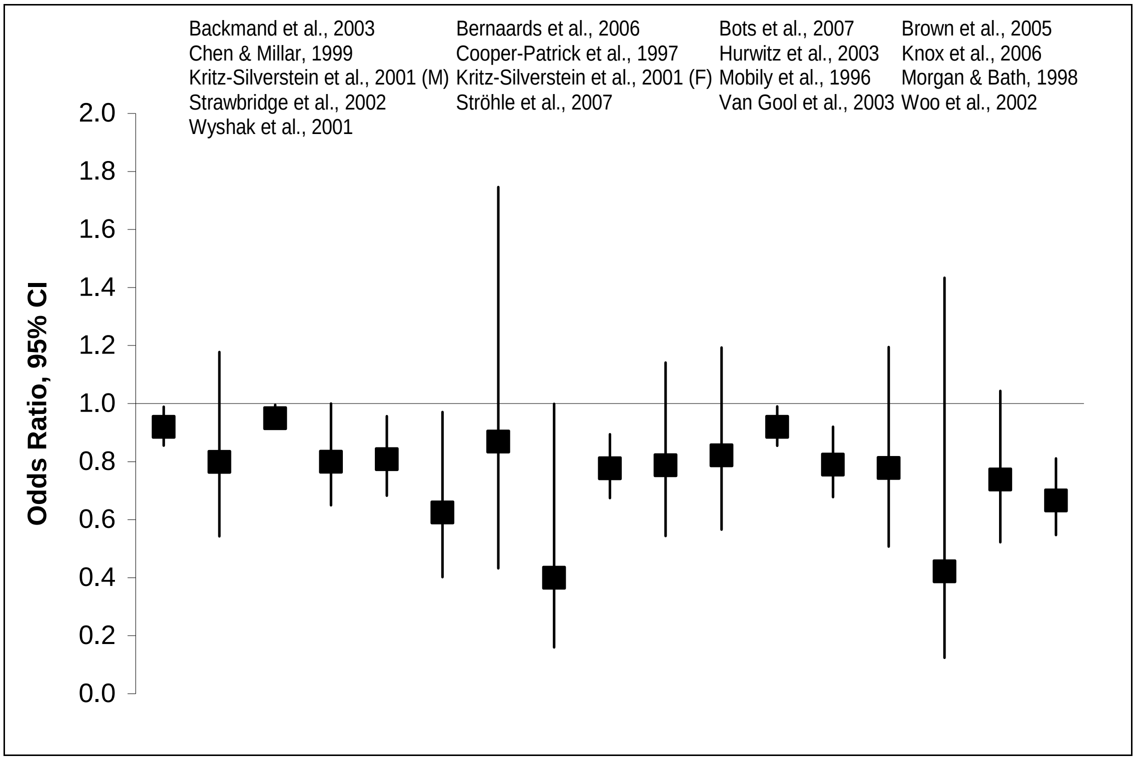

Figure G8.1b Data Points

Author/Date	High	Low	Odds Ratio
Backmand et al., 2003	0.9892	0.8556	0.92
Bernaards et al., 2006	1.1774	0.5429	0.7995
Bots et al., 2007	0.9956	0.9554	0.95
Brown et al., 2005	1	0.65	0.8
Chen & Millar, 1999	0.957	0.6831	0.8086
Cooper-Patrick et al., 1997	0.9714	0.4021	0.625
Hurwitz et al., 2003	1.7464	0.4326	0.8692
Knox et al., 2006	0.999	0.1602	0.4
Kritz-Silverstein et al., 2001 (M)	0.8946	0.6746	0.7769
Kritz-Silverstein et al., 2001 (F)	1.141	0.5439	0.7878
Mobily et al., 1996	1.1928	0.5659	0.8216
Morgan & Bath, 1998	0.99	0.855	0.92
Strawbridge et al., 2002	0.9205	0.678	0.79
Ströhle et al., 2007	1.1945	0.5072	0.7784
Van Gool et al., 2003	1.4337	0.1242	0.422
Woo et al., 2002	1.0435	0.5224	0.7383
Wyshak et al., 2001	0.8114	0.5472	0.6663

for a clinically meaningful decrease in symptoms (50%) or remission (32;35;37;38). Long-term reductions in symptoms were examined in a few studies and were generally favorable after supervised exercise training ended, especially when people maintained regular physical activity (28;29;36;39). The trial by Dunn and colleagues. (2005) was a placebo trial that controlled for social interaction and sunlight exposure (2 confounders common in other studies) and reported response and remission rates after exercise training that were 40 to 50% better than placebo (32).

Rationale: Healthy Adults and Adults With Medical Conditions

At least 42 RCTs since 1995, including more than 2,600 people, have examined the effects of exercise on depression symptoms in healthy adults or adults with medical conditions other than depression or disabling conditions that severely limit physical activity (i.e., spinal cord injury, multiple sclerosis, and stroke or traumatic head injury). Most of the medical patients studied had cardiovascular diseases, arthritis, chronic pain, obesity, or were cancer survivors. The mean effect of exercise compared to a control condition was 0.35 SD (95% CI: 0.24 to 0.46). The outcomes favored exercise in 90% (34 of 38) of the comparisons with control conditions, of which 60% (23 of 38) reached statistical significance. The average sample size was about 65 people, but in about a fourth of the studies it was less than 35, which was too small to detect an effect smaller than a half standard deviation (SD). When compared to a placebo (usually stretching or health education), the effect of exercise was halved to 0.15 SD (95% CI: 0.24 to 0.06). Although exercise effects exceeded placebo effects in 19 of 22 comparisons, only 4 reached statistical significance. The average sample size in the placebo studies was nearly 100 people, but samples more than 4 times that size would be needed to detect an effect that small.

Do the Effects of Physical Activity on Depression Symptoms Differ According to Age, Sex, Race/Ethnicity, or Medical Condition?

Conclusions

The available evidence supports the conclusion that regular physical activity reduces depression symptoms regardless of age, sex, race/ethnicity, or medical condition. Whether these factors modify the association between physical activity and depression has been understudied. Also, race and ethnicity have been poorly represented or not described in most studies.

Rationale: Cohort Studies

Few prospective cohort studies reported findings according to sex or age groups. Just 1 study reported results for men and women, finding that lower levels of depression symptoms were associated with more physical activity in both men and women (40). Only 11 studies had separate results for men or women. Reductions were smaller for active men (OR = 0.96, 95% CI = 0.93 to 0.99) than women (OR = 0.72, 95% CI = 0.68 to 0.77), but men were less studied. Five studies totaled fewer than 4,000 men, while 6 studies totaled more than 14,000 women. After adjusting for the number of comparisons made in each of the other cohort studies, in which men and women were represented evenly, effects for men and women did not differ. Crude odds reduction among active people were greater for people aged 55 years or older (OR = 0.58; 95% CI = 0.46 to 0.72) than people younger than age 55 year (OR = 0.72; 95% CI = 0.64 to 0.81), but physical activity was protective for all age groups, regardless of sex.

Most of the prospective cohort studies were population-based, but only a third specified the proportions of racial and ethnic groups included, and only 4 studies had evidence of good representation of African Americans and/or Hispanics/Latinos (41-44). One study reported that the odds of depression symptoms were similarly lower among white and African American adults who were active (42). Other studies had poor or no representation of other minority groups.

Rationale: Randomized Controlled Trials

In RCTs of people without depression, the average effect of exercise compared to a control condition is 0.35 SD in people with medical conditions (24 studies; 95% CI: 0.47 to 0.23) and 0.35 SD in people who have not been diagnosed with a medical condition (7 studies; 95% CI: 0.59 to 0.11). Figure G8.2 illustrates effect sizes and 95% confidence intervals comparing exercise with a control condition from the RCTs of depression in adults with or without medical conditions.

These trials reported similar reductions in depression for groups of varying ages from 28 to 83 years, but the studies were not designed to compare groups according to sex, race/ethnicity, or age. Only 1 of the trials compared men and women (45) and none compared effects between people of different ages or race/ethnicities. Seven of 11 studies of Americans described the racial/ethnic composition of their samples, but only 5 studies included African Americans (46-50); 3 studies included small numbers of Hispanics, Asian Americans or American Indians (49-51). Effects were larger in 6 studies of men (mean = 0.86 SD, 95% CI = 0.45 to 1.26), compared to 9 studies of women (mean = 0.27 SD, 95% CI = 0.04 to 0.51) and to 23 studies that combined results of men and women (mean = 0.27 SD, 95% CI = 0.16 to 0.37). Thus, it is likely that other features of the studies of men might explain the larger effects.

Reductions in depression symptoms were larger in 8 studies of heart patients (mean = 0.60 SD, 95% CI = 0.33 to 0.86) than in studies of other medical conditions (mean = 0.23 SD, 95% CI = 0.11 to 0.34) and were largest in the 3 studies of heart patients that included only men (52-54) (mean = 1.0 SD, 95% CI = 0.50 to 1.5). The small number of studies precluded meaningful comparisons among the other medical conditions.

Figure G8.2 Depression Symptoms: Randomized Controlled Trials, 1995 Through 2007

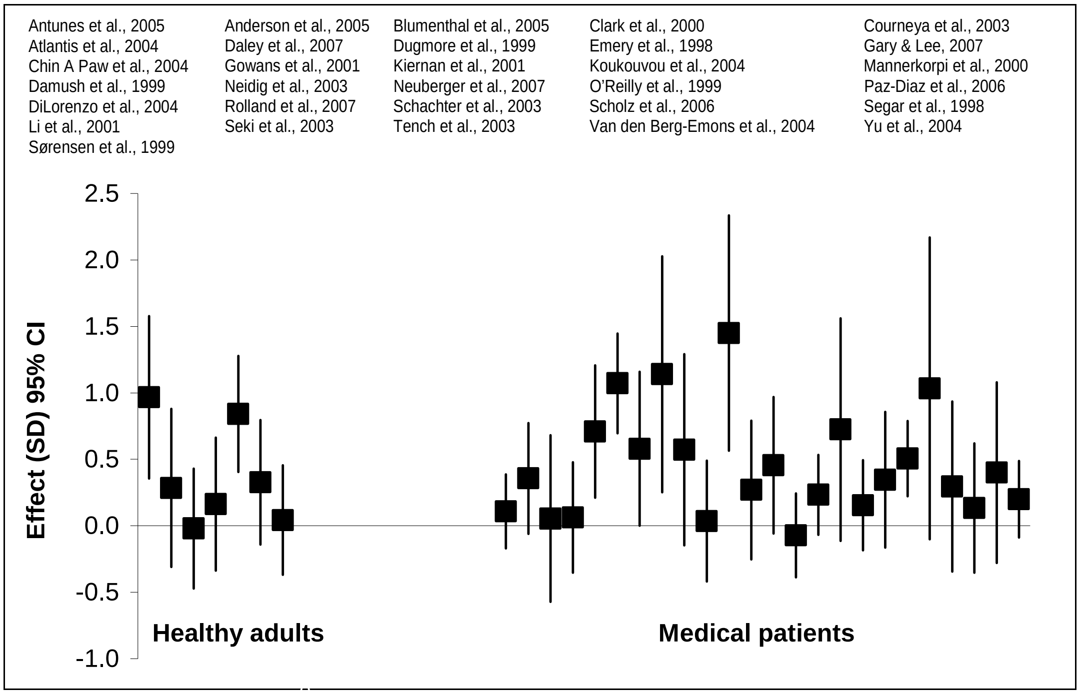

Figure G8.2. Data Points

Healthy Adults	High	Low	Effect Size
Antunes et al., 2005	1.5775	0.3545	0.966
Atlantis et al., 2004	0.8808	−0.3108	0.285
Chin A Paw et al., 2004	0.4298	−0.4718	−0.021
Damush et al., 1999	0.6628	−0.3368	0.163
DiLorenzo et al., 2004	1.2781	0.4039	0.841
Li et al., 2001	0.7952	−0.1406	0.3273
Sørensen et al., 1999	0.4545	−0.3687	0.0429

Medical Patients	High	Low	Effect Size
Anderson et al., 2005	0.3863	−0.1703	0.108
Blumenthal et al. 2005	0.7735	−0.0615	0.356
Clark et al., 2000	0.6815	−0.5729	0.0543
Courneya et al., 2003	0.4774	−0.3524	0.0625
Daley et al., 2007	1.2058	0.2102	0.708
Dugmore et al., 1999	1.4473	0.6947	1.071
Emery et al., 1998	1.1587	0.0003	0.5795
Gary & Lee, 2007	2.0279	0.2521	1.14
Gowans et al., 2001	1.2908	−0.1478	0.5715
Kiernan et al., 2001	0.4897	−0.4197	0.035
Koukouvou et al., 2004	2.3344	0.5646	1.4495
Mannerkorpi et al., 2000	0.7909	−0.2519	0.2695
Neidig et al., 2003	0.97	−0.059	0.4555
Neuberger et al., 2007	0.2436	−0.3876	−0.072
O'Reilly et al., 1999	0.5329	−0.0669	0.233
Paz-Diaz et al., 2006	1.561	−0.1128	0.7241
Rolland et al., 2007	0.4932	−0.185	0.1541
Schachter et al., 2003	0.8583	−0.1649	0.3467
Scholz et al., 2006	0.7897	0.2233	0.5065
Segar et al., 1998	2.1691	−0.1017	1.0337
Seki et al., 2003	0.935	−0.3452	0.2949
Tench et al., 2003	0.6196	−0.3542	0.1327
Van den Berg-Emons et al., 2004	1.0801	−0.2801	0.4
Yu et al., 2004	0.4876	−0.0886	0.1995

Do the Effects of Physical Activity Vary According to Features of Physical Activity, Including Type, Intensity, or Timing (i.e., Session Duration, Weekly Frequency, and Length of Participation)?

Conclusions

The evidence from prospective cohort studies and RCTs published since 1995 suggests that moderate and high levels of physical activity similarly reduce the odds of developing depression symptoms compared to low levels of physical activity exposure, which is nonetheless more protective than inactivity or very low levels of physical activity. The minimal or optimal type or amount of exercise for reducing depression symptoms is not yet known, but it appears that an increase in physical fitness is not required.

Rationale

Epidemiologic studies typically use a variety of criteria and methods to classify people into 2 or more activity groups. This limits the evaluation of the dose-response relation across the full range of reported physical activity and can misclassify people who overestimate or underestimate their activity. Only 7 prospective cohort studies of depression symptoms included the 3 or more levels of physical activity necessary to determine whether the association of physical activity with lower odds of depression has a dose-gradient with increased levels of exposure (16;18;21;22;55-57). After adjustment for age, sex, and other risk factors, the reduction of odds was smaller for the lowest level of physical activity (OR = 0.86, 95% CI = 0.79 to 0.94) compared to the next 2 levels of physical activity, which did not differ (OR = 0.77, 95% CI = 0.72 to 0.82). Thus, the highest levels of participation did not confer more protective benefits than did more moderate levels. Each was more protective than the lowest levels in the studies.

Figure G8.3 shows the odds ratios and 95% CI in prospective cohort studies that examined the dose-response association between levels of physical activity and depression symptoms.

Those studies used different measures and criteria for defining levels of physical activity, so it is not possible to convert their findings to a standard estimate (e.g., MET-hours or kilocalories per kilogram) of the amount of physical activity at each level. However, about half the prospective cohort studies provided enough information to determine whether active people were meeting existing public health recommendations (58;59) for participation in moderate or vigorous physical activity (i.e., moderate-intensity aerobic [endurance] physical activity for a minimum of 30 minutes on 5 days per week, or vigorous-intensity aerobic physical activity for a minimum of 20 minutes on 3 days per week). Odds reduction favored people who met or exceeded recommendations for moderate or vigorous participation (OR = 0.64, 95% CI = 0.57 to 0.73) compared to active people who did not meet either recommended level (OR = 0.70, 95% CI = 0.58 to 0.82). Odds were not different between vigorous and moderate participation, but it was possible to distinguish moderate from vigorous participation in only a few studies. After adjustment for other risk factors, a similar

Figure G8.3 Depression Symptoms: Prospective Cohort Studies 1995 Through 2007: Dose Response

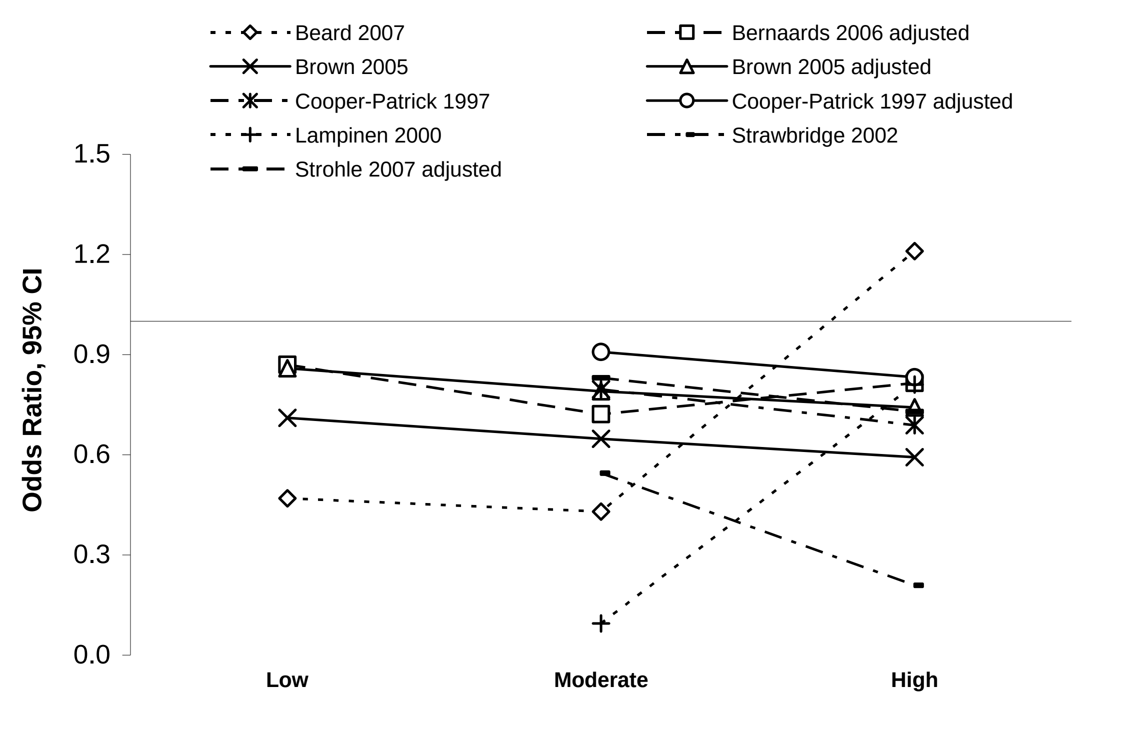

Figure G8.3 Data Points

Author/Year	Low	Moderate	High
Beard 2007	0.47	0.43	1.21
Bernaards 2006 adjusted	0.8694	0.7218	0.8151
Brown 2005	0.711	0.648	0.593
Brown 2005 adjusted	0.859	0.79	0.742
Cooper-Patrick 1997	0.796	0.689	
Cooper-Patrick 1997 adjusted	0.908	0.832	
Lampinen 2000	0.095	0.81	
Strawbridge 2002		0.545	0.209
Strohle 2007 adjusted	0.8303	0.7298	

protective benefit favored regular participation in moderate or vigorous physical activity (OR = 0.77, 95% CI = 0.72 to 0.82) compared to participation at levels less than recommended (OR = 0.84, 95% CI = 0.78 to 0.90).

A few RCTs of people without depressive disorders have manipulated type (e.g., aerobic versus resistance or walking versus aquatic exercise or Qigong) or timing (i.e., continuous versus intermittent [the intermittent studies often used resistance, circuit, interval or mixed-mode exercise]), of exercise to examine whether those features modify the effects of exercise on symptoms of depression (60-64). However, these studies did not include a control group who did not exercise. Only a few studies have evaluated Eastern health practices that include exercise (65). About 40 percent of the studies used an aerobic exercise intervention such as walking, jogging, cycling, or aquatic exercise, and another third of the studies combined aerobic activity with resistance exercise. Only 3 studies used resistance exercise alone, and none compared aerobic versus resistance exercise. On average, reductions in depression have been similar regardless of the mode of activity used. About two-thirds of the studies used continuous exercise. Regardless of mode, a larger reduction in depression tends to occur after continuous exercise (0.45 SD, 95% CI = 0.63 to 0.27) than intermittent exercise (0.18 SD, 95% CI = 0.30 to 0.06), but differing features of the studies other than timing might explain this finding.

Three-fourths of the RCTs of healthy adults and non-psychiatric medical patients used a moderate-to-vigorous exercise intensity of 60-80% of people's aerobic capacity or maximum strength that occurred 3 days per week. Intensity was lower or the frequency was 2 days per week in the other studies. The average duration of each session was about 35 minutes, but it was less than 30 minutes in a fourth of the studies and more than 1 hour in another fourth of the studies. However, fewer than half the studies were clear about how the time was partitioned into warm-up, exercise, and cool down. Nonetheless, reductions in depression symptoms did not differ across these varying features of exercise. Studies lasted an average of 6 months, and a fourth of the studies lasted less than 3 months. Length of the exercise program also was unrelated to symptom outcome. About half the studies measured cardiorespiratory fitness, which was increased significantly in 16 of 24 comparisons. Only 3 studies measured strength. In each study, fitness increases and symptom reduction were not associated when changes were defined by statistical significance, which depends on both the size of change and the sample size. After adjusting for sample sizes, the magnitude of depression reduction was moderately correlated with the magnitude of fitness increase ($r = 0.40$). However, that relation was not independent of increases in primary outcomes other than fitness in the studies of medical patients.

Perhaps the clearest experimental evidence for a dose-dependent effect of exercise on symptom reduction comes from the dose study (32). Adults aged 20 to 45 years diagnosed with mild to moderate major depressive disorder expended either 7.0 or 17.5 kilocalories per kilogram per week at a frequency of 3 or 5 days per week or engaged in 3 days per week of stretching exercises as a placebo control. Physician-rated symptoms after 12 weeks were reduced 47% from baseline for the higher dose, compared with 30% for the lower dose and 29% for control, regardless of whether exercise frequency was 3 days or 5 days each week.

Question 2. Is There an Association Between Physical Activity and Anxiety?

Introduction

Anxiety is characterized by apprehensive or worrisome thoughts and is typically accompanied by agitation, feelings of tension, and activation of the autonomic nervous system. A distinction is made between transient anxiety symptoms, termed *state anxiety*, persistent symptoms, termed *trait anxiety*, and a group of disabling conditions characterized by excessive, chronic anxiety that are known as *anxiety disorders*. The anxiety disorders, listed from most to least common, are:

- *Specific phobia* — an intense fear of an object, place, or situation that poses little or no actual danger.
- *Social phobia* — an overwhelming fear of scrutiny and embarrassment in social situations, leading to avoidance of potentially enjoyable activities.
- *Generalized anxiety disorder* — recurrent or persistent excessive worry about everyday, routine life events and activities, lasting at least 6 months.
- *Panic disorder* — repeated episodes of intense fear and physical symptoms that strike without warning and without an obvious source, often producing fear of being alone or going into public places (*agoraphobia*) and persistent fear of an attack.
- *Obsessive-compulsive disorder* — repeated, unwanted thoughts or compulsive behaviors that seem impossible to stop, typified by repetitive acts or rituals to relieve anxiety.
- *Post–traumatic stress disorder* — a delayed or prolonged response (including flashbacks, dreams, insomnia, hypervigilance) to a stressful event or situation (either short- or long-lasting) that was especially threatening or catastrophic (6).

Anxiety disorders are common, affecting more than 16 million people in the United States each year (roughly 4% of women and 2% of men). More than 80 million people in the United States at some point in their lives suffer from an anxiety disorder (8). Anxiety disorders begin at a median age of 15 years, often persist throughout life and are associated with numerous physical and mental co-morbidities, especially depression (66). People aged 15 to 24 years experience episodes of anxiety about 40% more often than people aged 25 to 54 years, regardless of race. Although less than 30% of those who suffer from anxiety disorders seek treatment, they strain the health care system because of direct psychiatric and nonpsychiatric treatment costs. Additional indirect costs of anxiety disorders are incurred from reduced work productivity. The total annual costs in 1990 of all anxiety disorders were estimated to be $42 billion to $47 billion dollars (67;67;68), and they likely cost double that amount today.

Does Physical Activity Protect Against the Onset of Anxiety Disorders or Anxiety Symptoms?

Conclusions

The weight of evidence from a small number of nationally representative and population-based cross-sectional and prospective cohort studies supports that regular physical activity protects against the onset of anxiety disorders and anxiety symptoms.

Rationale

At least 4 population-based cross sectional studies published since 1995, including data from nationally representative samples of nearly 121,000 Americans, show that regular physical activity is associated with lower odds of anxiety symptoms (13;69-71). Results of the US National Co-Morbidity Study found that regular physical activity reduced the odds of a diagnosed anxiety disorder (i.e., specific phobia, social phobia, generalized anxiety, panic, and agoraphobia) by an average of 43% (10). After controlling for sociodemographic and illness variables, regular physical activity reduced the odds of an anxiety disorder by an average of 28% (10).

At least 2 population-based studies used a prospective cohort design. The odds of developing any anxiety disorder were reduced by an average of 53% among Australians who reported more than 3 hours per week of vigorous physical activity compared to those reporting no activity (16). The effect was not statistically significant, in part due to the small number of participants who developed an anxiety disorder (n=67). The second study, which adjusted for age and sex and had more participants who developed an anxiety disorder (n=228), found that regularly active young adults (representative of Munich, Germany) on average had a statistically significant, 48% lower odds of developing any anxiety disorder compared to those reporting no activity (22).

Does Physical Activity Reduce Anxiety Symptoms?

Conclusions

The results of RCTs conducted with medical patients and healthy adults indicate that participation in physical activity programs reduces anxiety symptoms.

Rationale

Before 1995, no reports of RCTs of anxiety disorder patients had been reported. Since then, 2 RCTs have been conducted with anxiety disorder patients and reported statistically large effects. One trial conducted with 46 panic disorder patients found that those who completed a 10-week (3 times per week) walking or jogging program reported, on average, a large reduction in anxiety symptoms (1.1 SD) compared to those who took daily placebo capsules (72). The other trial involved 74 patients with social phobia, generalized anxiety, or panic disorder. The addition of a moderate intensity home-based exercise program to 8 to 10 weeks of group cognitive-behavioral therapy (GCBT) resulted in a large reduction in anxiety symptoms (1.36 SD) compared to the control condition (GCBT + nutrition education) after statistically controlling for potential confounding variables (73).

Before 1995, at least 40 quasi-experimental and experimental exercise training studies of varying quality had reported a cumulative effect on reducing anxiety symptoms of approximately 0.40 SD (74). Since 1995, at least 46 RCTs involving more than 3,550 people have examined the effects of chronic exercise on anxiety symptoms among inactive adults who were healthy or had a medical condition other than anxiety disorders or disabling CNS disorders including multiple sclerosis, traumatic head injury, stroke or spinal cord injury. The effect of exercise compared to control conditions in reducing anxiety symptoms was 0.38 SD (95% CI: 0.30 to 0.46). Outcomes favored exercise in 84% (67 of 80) of the comparisons with control conditions, and 28% (22 of 80) reached statistical significance. In 6 studies that compared moderate-to-vigorous exercise to a placebo-type condition (usually low intensity exercise such as stretching) the effect of moderate-to-vigorous exercise on reducing anxiety symptoms was 0.19 SD (95% CI: 0.05 to 0.33). Exercise effects were favorable in 90% (9 of 10) of the placebo-type comparisons, and 30% reached statistical significance. The average study included about 60 people, but a fourth of the studies had less than 40 participants, too few to detect small but possibly meaningful effects.

Do the Effects of Physical Activity on Anxiety Symptoms Differ According to Age, Sex, Race/Ethnicity, or Medical Condition?

Conclusions

The weight of the evidence supports the conclusion that regular physical activity reduces anxiety symptoms regardless of age, sex or medical condition. No published data address whether race or ethnicity modifies the effects of physical activity on anxiety symptoms.

Rationale

In the 46 RCTs of healthy adults and medical patients, the mean age of the samples was weakly related to anxiety reductions after exercise training. Two of the trials compared men and women and found no sex-related difference in the effect of exercise on anxiety symptoms (45;75). The average effect of exercise training on reduced symptoms of anxiety was larger in those studies that involved only men (mean = 0.62 SD, 95% CI: 0.34 to 0.89, n=7) compared to those that included only women (mean = 0.33 SD, 95% CI: 0.16 to 0.50, n=12) and those that included similar proportions of men and women (mean = 0.42 SD, 95% CI: 0.28 to 0.57, n=19). It is likely that other features of the studies of men might explain the larger effects. Regardless, exercise benefited both men and women.

None of the available investigations was designed to determine whether the effect of chronic exercise was moderated by race or ethnicity. The racial or ethnic composition of the samples was described in 17% of the reviewed studies (25;51;76-81). Of the 3,550 people who participated in the RCTs, approximately 89% were whites and approximately 11% were African Americans or Hispanics. Statistical analyses by race or ethnic category were not presented in any of the studies.

Of the RCTs, about 40% (19 of 46) were conducted with healthy adults, and 60% (27 of 46) involved patients with various medical conditions. The most frequently studied conditions were cancer and cardiovascular diseases. The average effect of exercise compared to a control condition was 0.40 SD in healthy adults (40 comparisons; 95% CI: 0.27 to 0.53) and 0.36 in people with medical conditions (40 comparisons; 95% CI: 0.26 to 0.47). The reduction in anxiety symptoms was somewhat larger than average in studies of cardiovascular conditions (mean = 0.53 SD, 95% CI: 0.15 to 0.92, n=6), but too few studies are available to conclude that the effect of exercise training on anxiety symptoms is modified by medical condition. Figures G8.4a and G8.4b summarize the findings from the RCTs of physical activity and anxiety symptoms in healthy adults and medical patients.

Epidemiologic studies have not yet examined race/ethnicity or medical condition as potential modifiers of the effect of exercise on anxiety disorders or symptoms. One cross-sectional study of 41,914 participants in the 2001 Behavioral Risk Factor Surveillance System found low anxiety symptoms among physically active people compared to inactive people across young (age 18 to 40 years), middle-aged (aged 41 to 60 years) and older adult (aged 61 years and older) categories, but the inactive younger adults were approximately 20% more likely to experience anxiety symptoms than inactive middle-aged and older adults (13). In a population-based cross sectional study of 19,288 twins and their families, potential interactions of exercise and age, exercise and sex and exercise, age and sex on anxiety symptoms were statistically non-significant (69).

Do the Effects of Physical Activity Vary According to Features of Physical Activity Including Type, Intensity, or Timing (i.e., Session Duration, Weekly Frequency, and Length of Participation)?

Conclusions

Limited cross-sectional, observational evidence suggests that the odds of an anxiety disorder may be reduced by higher weekly frequency of exercise bouts. However, there is an absence of evidence from prospective cohort studies or RCTs that examine whether anxiety symptoms vary according to features of physical activity exposure.

Rationale

One large population-based study found a dose-response relation between cross-sectional measures of physical activity frequency and lower prevalence of anxiety disorders (i.e., specific phobia, social phobia, generalized anxiety, panic, and agoraphobia) (10). The

Figure G8.4a Anxiety Symptoms: Randomized Controlled Trials of Healthy Adults 1995 Through 2007

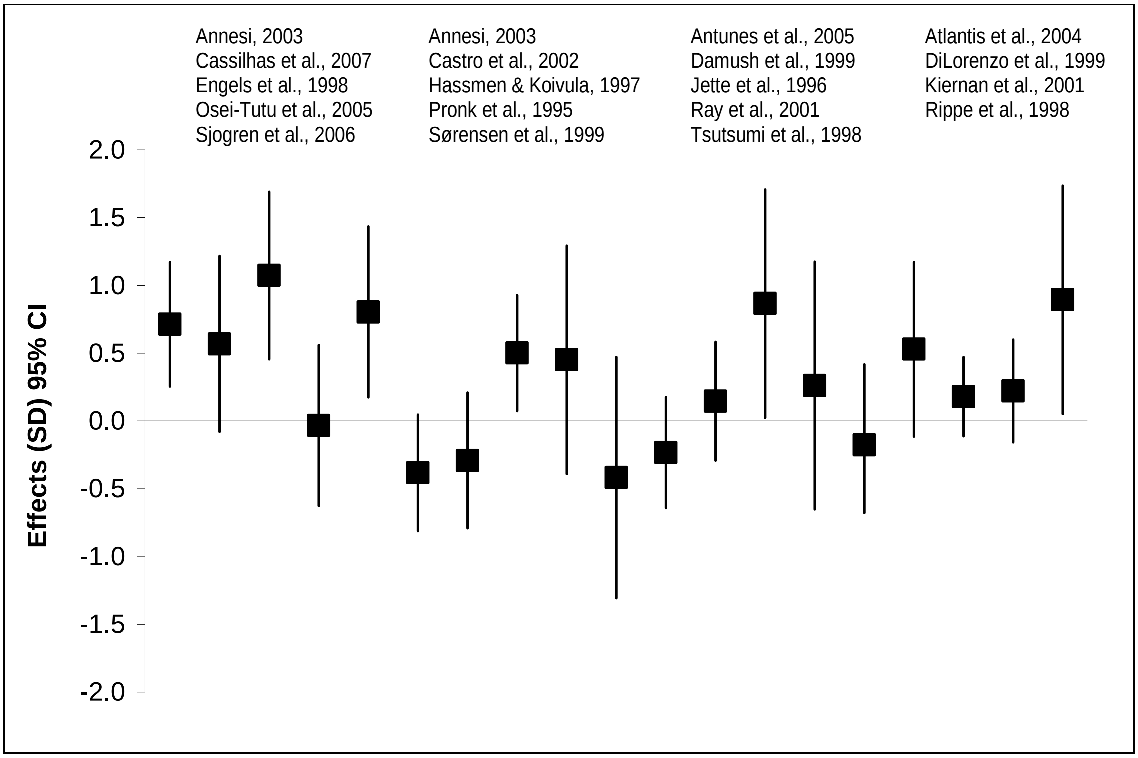

Figure G8.4a Data Points

Author	Year	High	Low	Effect Size
Annesi	2003	1.1726	0.2534	0.713
Annesi	2003	1.2184	−0.0811	0.5687
Antunes et al.	2005	1.6922	0.4556	1.0739
Atlantis et al.	2004	0.5596	−0.6273	−0.0339
Cassilhas et al.	2007	1.4338	0.1748	0.8043
Castro et al.	2002	0.047	−0.8126	−0.3828
Damush et al.	1999	0.2104	−0.7926	−0.2911
DiLorenzo et al.	1999	0.9291	0.072	0.5006
Engels et al.	1998	1.2926	−0.3902	0.4512
Hassmen & Koivula	1997	0.4711	−1.3073	−0.4181
Jette et al.	1996	0.1764	−0.6431	−0.2334
Kiernan et al.	2001	0.5843	−0.2918	0.1463
Osei-Tutu et al.	2005	1.7087	0.0233	0.866
Pronk et al.	1995	1.1766	−0.6525	0.262
Ray et al.	2001	0.4161	−0.6794	−0.1767
Rippe et al.	1998	1.1732	−0.1149	0.5292
Sjogren et al.	2006	0.472	−0.1135	0.1792
Sørensen et al.	1999	0.6008	−0.159	0.2209
Tsutsumi et al.	1998	1.7363	0.052	0.8946

Figure G8.4b. Anxiety Symptoms: Randomized Controlled Trials of Medical Patients 1995 Through 2007

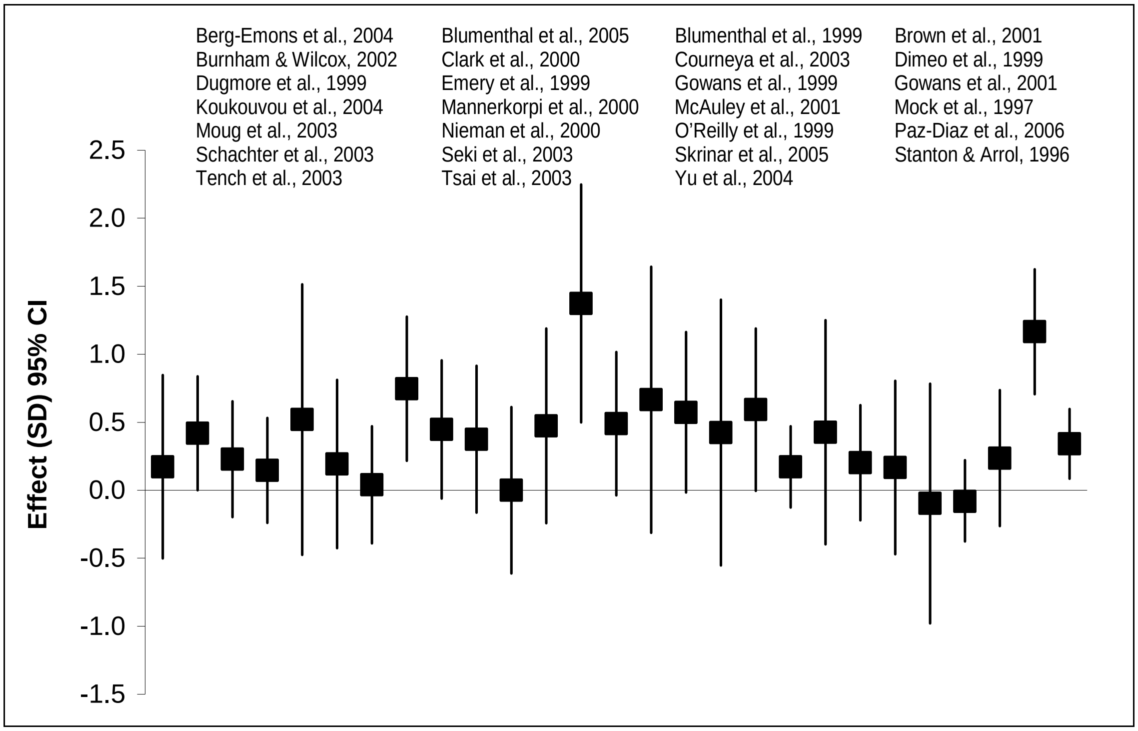

Figure G8.4b Data Points

Author	Year	High	Low	Effect Size
Berg-Emons et al.	2004	0.8471	−0.5021	0.1725
Blumenthal et al.	2005	0.8372	0	0.4186
Blumenthal et al.	1999	0.6547	−0.1989	0.2279
Brown et al.	2001	0.532	−0.2394	0.1463
Burnham & Wilcox.	2002	1.5144	−0.4748	0.5198
Clark et al.	2003	0.812	−0.4264	0.1928
Courneya et al.	2000	0.471	−0.3913	0.0399
Dimeo et al.	1999	1.2758	0.2166	0.7462
Dugmore et al.	1999	0.9564	−0.0625	0.447
Emery et al.	1999	0.9157	−0.1661	0.3748
Gowans et al.	1999	0.6123	−0.6124	0
Gowans et al.	2001	1.1875	−0.2423	0.4726
Koukouvou et al.	2004	2.2472	0.4995	1.3733
Mannerkorpi et al.	2000	1.0158	−0.039	0.4884
McAuley et al.	2001	1.6432	−0.3133	0.665
Mock et al.	1997	1.1626	−0.0178	0.5724
Moug et al.	2003	1.3995	−0.5531	0.4232
Nieman et al.	2000	1.1882	−0.004	0.5921
O'Reilly et al.	1999	0.4695	−0.1279	0.1708
Paz-Diaz et al.	2006	1.25	−0.3972	0.4264
Schachter et al.	2003	0.6268	−0.2207	0.2031
Seki et al.	2003	0.8051	−0.4711	0.167
Skrinar et al.	2005	0.7841	−0.9789	−0.0974
Stanton & Arrol.	1996	0.2212	−0.3778	−0.0829
Tench et al.	2003	0.7356	−0.2636	0.236
Tsai et al.	2003	1.6238	0.7053	1.1645
Yu et al.	2004	0.5979	0.0852	0.3415

percentage of adults with these anxiety disorders was highest among those who reported no physical activity and was reduced in a step-wise fashion among those who reported rare, occasional, and regular physical activity (10).

Prospective cohort studies show mixed results as to whether participation in sports, activities that often involve high-intensity exercise, has a protective effect against anxiety symptoms. Some show a protective effect (23) and others show no protection (82). One nationally representative cross-sectional study found that a group of regularly physically active (i.e., met or exceeded the *Healthy People 2010* physical activity guidelines) people reported a higher frequency of anxiety symptoms compared to those who were physically active but not active enough to meet the *Healthy People 2010* recommendations (13).

Few RCTs of healthy adults or people with medical conditions have manipulated any feature of an exercise intervention to learn whether those features causally modify anxiety symptoms. No exercise training studies have manipulated exercise program length or exercise type for the purpose of examining anxiety symptom outcomes.

About 43% (20 of 46) of the studies used a single aerobic exercise intervention such as walking, jogging, or cycling, 13% (6 of 46) used resistance exercise alone, and 9% (4 of 46) combined aerobic with resistance exercise. The magnitude of anxiety reduction has been similar across these 3 categories of studies. Regardless of mode, anxiety reductions also were similar after continuous (0.36 SD, 95% CI: 0.27 to 0.45) and intermittent (0.39 SD, 95% CI: 0.16 to 0.63) exercise (about 60% of studies used continuous exercise).

Three investigations manipulated exercise session duration and found no significant differences in anxiety symptom outcomes among exercise training studies that used bouts of varying session durations (80;83;84). Across all trials, the average duration of the exercise sessions was approximately 40 minutes. In a fourth of the studies, the duration was less than 25 minutes, and in another fourth the duration was more than 60 minutes. The effects of exercise training on anxiety symptoms were similar across studies of all durations. Imprecise descriptions of exercise duration contributed to the difficulty in determining whether session duration has a true effect. For example, less than half of the studies were specific regarding how time was partitioned into warm-up, exercise, and cool down.

Only 2 exercise training experiments manipulated exercise intensity to examine whether it modifies the effects of exercise on anxiety symptoms. Statistically non-significant differences in anxiety symptoms were found between moderate- and high-intensity resistance exercise conditions on the anxiety symptom outcomes (81;85). About 55% (44 of 80) of the comparisons from all the trials used moderate-to-vigorous exercise intensity (i.e., 60 – 80% of aerobic capacity or maximum strength) with a weekly frequency of 3 or more days per week. Reductions in anxiety symptoms were similar across variations in exercise intensity.

About 63% (29 of 46) of the trials measured fitness, 7 studies measured strength, and 22 studies measured cardiorespiratory fitness. Cardiorespiratory fitness was increased significantly in 36% (13 of 36) of the comparisons and strength was increased significantly in 25% (2 of 8) of the comparisons. Those studies that defined changes by statistical significance showed no association between fitness increases and anxiety symptom reduction. After adjusting for sample sizes, the magnitude of anxiety reduction was weakly correlated with the magnitude of fitness increase (r = .24). This relation was independent of increases in primary outcomes other than fitness in the studies.

Question 3: Is There an Association Between Physical Activity and Psychological Distress and Well-Being?

Introduction

Psychological distress is a risk factor for psychiatric disorders (86;87) and coronary heart disease (88), and it is negatively associated with quality of life. Conversely, a feeling of well-being can reduce psychiatric risk and is an important feature of high life quality and health (89). People frequently experience feelings of distress during the normal course of living and during challenging life events, including chronic medical conditions. Thus, it is important to understand the association between physical activity and feelings of distress or well-being because they bear not only on disease risk but also on overall mental health. Measures in this area are not uniform, but most studies have used a scale that assessed the presence of distress (e.g., combined symptoms of anxiety and depression or perceived stress) or the absence of distress (e.g., well-being or positive mental health). Findings of physical activity studies have not differed when measures of distress or well-being were used, so the following results apply regardless of the direction of odds (i.e., decrease in distress or increase in well-being).

Does Physical Activity Protect Against the Onset of Feelings of Distress or Enhance Well-Being?

Conclusions

The available evidence from prospective cohort studies indicates a small-to-moderate association that favors people who are physically active.

Rationale

The association between physical activity and reduced feelings of distress or enhanced well-being among adults was virtually unstudied in large groups of people before 1995 (90). Since then, more than 30 population-based observational studies have been published, including nationally representative samples of more than 175,000 Americans (91-95). Most of the studies looked at cross-sectional associations, which indicated that active people on average had more than a 30% lower odds of feeling of distress or 30% higher odds of enhanced well-being than did inactive people. In the national samples of Americans, the odds favored active people by approximately 25%.

Thirteen studies of adults in Australia, Canada, Denmark, England, Netherlands, Scotland, Wales, and 3 studies of Americans (18;23;94) used a prospective cohort design. In those studies, the average odds of reduced feelings of distress or of enhanced well-being favored active people by about 30% compared with inactive people, without adjustments for risk factors (OR = 0.69, 95% CI = 0.61 to 0.78). After adjustment for risk factors, such as age, sex, race, education, social class, occupation, income, smoking, alcohol use, substance abuse, chronic health conditions, disability, marital status, life events, job stress, and social support, the odds still favored active people by nearly 20% (OR = 0.82, 95% CI = 0.77 to 0.86). About 80% of the comparisons (58 of 70) favored active adults, but half the results did not reach statistical significance, often because of too small sample sizes. The average number of people for each comparison was approximately 1,300 people, but a fourth of the comparisons had 700 people or less. Figure G8.5 illustrates 18 crude and/or adjusted odds ratios and 95% confidence intervals from the 13 prospective cohort studies of physical activity and distress or well-being in more than 100,000 adults from 8 countries, including 67,000 American women (23;94).

Does Physical Activity Reduce Feelings of Distress or Enhance Feelings of Well-Being?

Conclusions

The effects of RCTs indicate small benefits of physical activity that often do not exceed the effects of placebo control conditions, such as health education or stretching.

Rationale

Since 1995, at least 26 RCTs, including nearly 3,000 people, have examined the effects of exercise on feelings of distress or well-being in healthy adults or adults with medical conditions other than psychiatric disorders or disabling conditions that severely limit physical activity (i.e., spinal cord injury, multiple sclerosis, and stroke or severe head trauma). The average effect of exercise compared to a control condition was 0.27 SD (95% CI = 0.16 to 0.38). The outcomes were favorable after exercise in nearly 80 percent of the comparisons (26 of 33) with control conditions, but only 13 of 33 comparisons reached statistical significance. The average sample size was about 60 people, but a fourth of the studies had less than 45, a much smaller number than the 200 or so people needed to detect an effect as small as one-third SD. When compared to a placebo (usually stretching or health education), the effect of exercise was reduced to 0.10 SD (95% CI: −0.12 to 0.32) and was significant in just 2 of 9 comparisons.

Figure G8.5 Feelings of Distress/Well-Being: Prospective Cohort Studies, 1995 Through 2007: Crude and Adjusted Odds

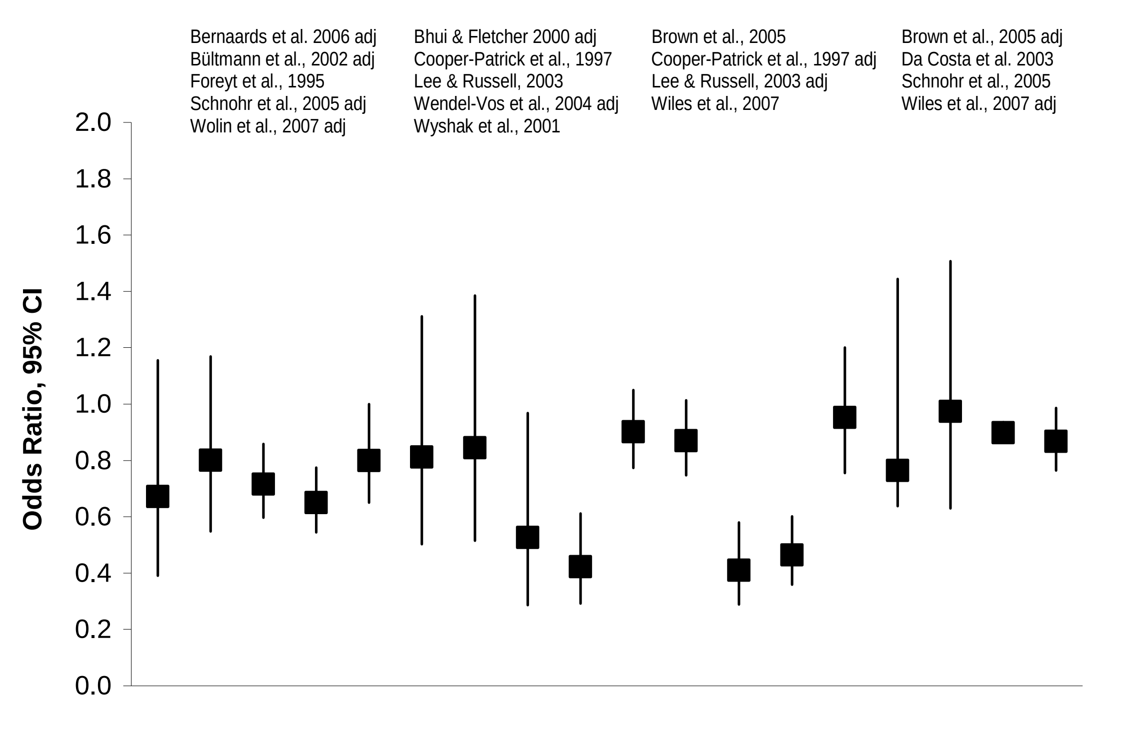

Figure G8.5 Data Points

Author	Year	High	Low	Odds Ratio
Bernaards et al.	2006 adj	1.155	0.391	0.6719
Bhui & Fletcher	2000 adj	1.169	0.548	0.8008
Brown et al.	2005	0.858	0.597	0.716
Brown et al.	2005 adj	0.775	0.545	0.65
Bültmann et al.	2002 adj	1	0.65	0.8
Cooper-Patrick et al.	1997	1.311	0.503	0.8118
Cooper-Patrick et al.	1997 adj	1.385	0.515	0.8444
Da Costa et al.	2003	0.968	0.287	0.527
Foreyt et al.	1995	0.611	0.292	0.4221
Lee & Russell	2003	1.05	0.774	0.9015
Lee & Russell	2003 adj	1.014	0.747	0.8699
Schnohr et al.	2005	0.58	0.289	0.4099
Schnohr et al.	2005 adj	0.601	0.359	0.4648
Wendel-Vos et al.	2004 adj	1.201	0.755	0.9521
Wiles et al.	2007	1.444	0.638	0.764
Wiles et al.	2007 adj	1.507	0.63	0.9741
Wolin et al.	2007 adj	0.935	0.863	0.8985
Wyshak et al.	2001	0.986	0.764	0.868

Do the Effects of Physical Activity on Distress or Well-Being Differ According to Race/Ethnicity, Sex, Age, or Medical Condition?

Conclusions

The available evidence supports that regular physical activity is associated with reduced feelings of distress and enhanced feelings of well-being regardless of age, sex, race/ethnicity, or medical condition. However, whether these factors modify those associations has not been studied. Race and ethnicity have been poorly represented or not described in most studies.

Rationale

Cross-sectional samples of Americans in the National Health Interview Survey (92), the Behavioral Risk Factor Surveillance Survey (93;95), and the National Physical Activity and Weight Loss Survey (91) included African American, Hispanics, and small numbers of Asian Americans and American Indians, but results were not compared between groups. Most of the prospective cohort studies were conducted in Europe or Australia and did not describe minority representation of the sample. The US Nurses' Health Study includes minority women, but their representation was not described in the study of physical activity and well-being in the cohort (94).

Similarly, it is unclear whether sex and age modify the protective effect of physical activity on distress/well-being. Only 4 cohort studies reported findings separately for males and females, with mixed results (96-99), and none compared age groups. Across cohort studies, findings were similar for men and women. However, age was inversely related to reduced odds of distress or increased odds of enhanced well-being regardless of sex. After adjustment for other risk factors, odds were 0.65 (95% CI = 0.61 to 0.72) for men and women younger than age 55 years and 0.90 (95% CI = 0.86 to 0.97) for men and women aged 55 years and older. In RCTs, the average effect of exercise compared to a control condition is similar in both healthy adults (0.28 SD, 95% CI = 0.16 to 0.41) and people with non-psychiatric medical conditions (0.26, 95% CI: 0.10 to 0.41). Figure G8.6 illustrates effect sizes and 95% confidence intervals feelings of distress or well-being in studies comparing exercise with a control condition from the RCTs of adults with or without medical conditions.

These trials reported similar effects of exercise in both men and women and in groups varying in mean aged 31 to 74 years. However, the studies were not designed to compare groups according sex, race/ethnicity, or age. Only 1 of the trials compared men and women (45), and results were mixed across the 3 studies of men (0.49 SD, 95% CI = −0.11 to 1.08). Ten studies reported results for women (0.21 SD, 95% CI = 0.02 to 0.40), and 15 studies combined results for similar proportions of men and women (0.26 SD, 95% CI = 0.12 to 0.41). None compared effects between people of different ages or race/ethnicities. Seven of 16 studies of Americans described the racial/ethnic composition of their samples, but only 2 studies included a substantial portion of African Americans

Figure G8.6 Feelings of Distress/Well-Being: Randomized Controlled Trials 1995 Through 2007

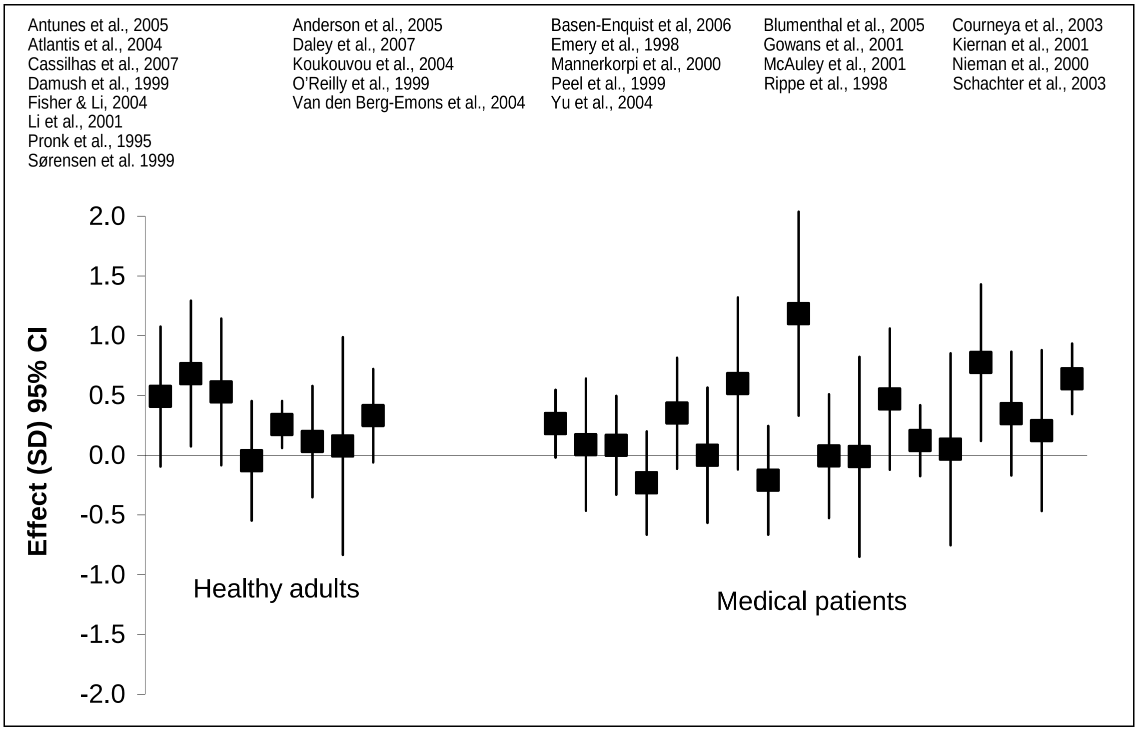

Figure G8.6 Data Points

Healthy Adults	Year	High	Low	Effect Size
Antunes et al.	2005	1.077	−0.095	0.491
Atlantis et al.	2004	1.293	0.073	0.683
Cassilhas et al.	2007	1.144	−0.084	0.53
Damush et al.	1999	0.453	−0.547	−0.047
Fisher & Li	2004	0.455	0.059	0.257
Li et al.	2001	0.58	−0.353	0.114
Pronk et al.	1995	0.987	−0.835	0.0758
Sørensen et al	1999	0.721	−0.059	0.331

Medical Patients	Year	High	Low	Effect Size
Anderson et al.	2005	0.549	−0.019	0.265
Basen-Enquist et al.	2006	0.641	−0.465	0.088
Blumenthal et al.	2005	0.496	−0.332	0.082
Courneya et al.,	2003	0.2	−0.666	−0.233
Daley et al.	2007	0.817	−0.115	0.351
Emery et al.	1998	0.566	−0.566	0
Gowans et al.	2001	1.319	−0.119	0.6
Kiernan et al.	2001	0.246	−0.666	−0.21
Koukouvou et al.	2004	2.037	0.331	1.1837
Mannerkorpi et al.	2000	0.511	−0.527	−0.008
McAuley et al.	2001	0.825	−0.85	−0.0123
Nieman et al.	2000	1.06	−0.121	0.4695
O'Reilly et al.	1999	0.42	−0.176	0.122
Peel et al.	1999	0.854	−0.754	0.05
Rippe et al.	1998	1.43	0.12	0.775
Schachter et al.	2003	0.866	−0.17	0.348
Van den Berg-Emons et al.	2004	0.88	−0.468	0.206
Yu et al.	2004	0.934	0.344	0.639

(46;100). Three studies included small numbers of Hispanics and/or Asian Americans (51;78;100). The small number of studies precluded meaningful comparisons among the medical conditions.

Do the Effects of Physical Activity Vary According to Features of Physical Activity Including Type, Intensity, or Timing (i.e., Session Duration, Weekly Frequency, and Length of Participation)?

Conclusions

Population-based studies indicate that participation in either moderate or high levels of physical activity is associated with reduced feelings of distress or enhanced well-being, when compared with inactivity or very low physical activity exposure. The minimal or optimal type or amount of exercise for reducing feelings of distress or enhancing feelings of well-being are not yet known, but it appears that an increase in physical fitness is not required.

Rationale

Seven prospective cohort studies of feelings of distress or well-being included 3 or more levels of physical activity, using inactivity or low activity as the reference group (18;55;56;94;96;97;101). Independently of age and sex, and with or without adjustment for other risk factors, a linear reduction in odds of about 10% occurred for each level of physical activity compared to people who were inactive or had very low activity. Similarly, odds favored people who met or exceeded recommendations for moderate or vigorous participation by about 5% compared to active people who did not meet either recommended level. No studies permitted a direct comparison of moderate and vigorous recommended levels, but unadjusted odds were lower for participation in moderate-to-vigorous physical activity (OR = 0.77, 95% CI = 0.70 to 0.84) compared to participation at levels less than recommended (OR = 0.84, 95% CI = 0.78 to 0.91). Figure G8.7 shows the odds ratios and 95% CI in prospective cohort studies that examined the dose-response association between levels of physical activity and feelings of distress or well-being.

A few RCTs manipulated type (walking versus aquatic exercise or Qigong) or timing (i.e., intermittent versus continuous) of exercise to examine whether those feature modify the effects of exercise on feelings of distress or well-being (60-62;64), but the studies did not include a control group who did not exercise. About 45 percent of the controlled studies used an aerobic exercise intervention such as walking, jogging, cycling, or aquatic exercise, and another 30 percent of the studies combined aerobic activity with resistance exercise. Only 3 studies used resistance exercise alone, and none compared aerobic with resistance exercise. About half the studies used continuous exercise, and a third used intermittent exercise. One study of home-based aerobic dance reported positive effects when daily exercise was a continuous 30-minute session but not when it was 2 sessions of 15 minutes each separated by 4 hours (80). Timing of the exercise could not be determined in the other studies. Effects of exercise did not differ according to the mode or timing of exercise.

Figure G8.7 Feelings of Distress/Well-Being: Prospective Cohort Studies 1995 Through 2007: Dose Response

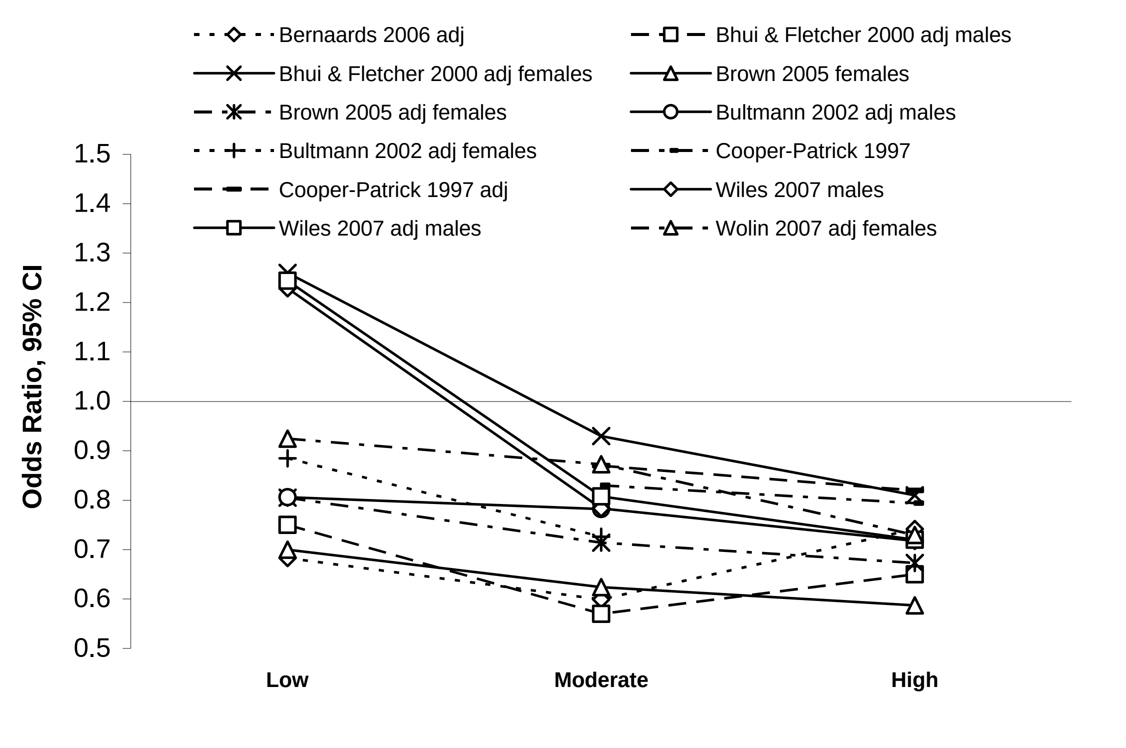

Figure G8.7 Data Points

Author/Year	Low	Moderate	High
Bernaards 2006 adj	0.6829	0.599	0.7416
Bhui & Fletcher 2000 adj males	0.75	0.57	0.65
Bhui & Fletcher 2000 adj females	1.26	0.93	0.81
Brown 2005 females	0.7	0.624	0.587
Brown 2005 adj females	0.805	0.714	0.673
Bultmann 2002 adj males	0.806	0.782	
Bultmann 2002 adj females	0.885	0.726	
Cooper-Patrick 1997		0.83	0.794
Cooper-Patrick 1997 adj		0.87	0.8196
Wiles 2007 males	1.2288	0.7833	0.7178
Wiles 2007 adj males	1.244	0.8079	0.72
Wolin 2007 adj females	0.9247	0.8729	0.7298

Three-fourths of the studies used a moderate-to-vigorous exercise intensity of 60% to 80% of people's aerobic capacity or maximum strength. The average session lasted 45 minutes and occurred 3 days per week, but studies had a wide range of session duration (10 to 85 minutes) and weekly frequency (1 to 7 days). Nonetheless, these features of exercise did not modify effects independently of each other. Studies lasted an average of 6 months, and a fourth of the studies lasted less than 3 months. Length of the exercise program was also unrelated to symptom outcome.

Eleven of 13 studies that measured cardiorespiratory fitness reported a significant increase that averaged 1 SD, or about 20%. Strength was significantly increased in each of 3 studies that measured strength. However, there was no association between fitness increases and changes in feelings of distress or well-being.

Question 4: Is There an Association Between Physical Activity and Cognitive Function and Dementia?

Introduction

Cognition can be conceptualized as processes involved in selecting, manipulating, and storing information derived from experiences and how these processes guide behavior. Cognitive abilities are functional properties of the individual that are not directly observed but are inferred from behavior. Researchers in the disciplines of psychometrics, cognitive psychology, and neuropsychology have developed more than 400 tests designed to assess specific types of mental processing (102). They range from those designed to evaluate specific processes (e.g., working memory, information-processing speed, inhibition) to those that assess global mental functioning involving multiple processes. Assessment methods include those designed specifically to evaluate the effects of injury and degenerative disease on cognitive function and those designed to evaluate individual differences in healthy individuals. The multidimensionality of cognitive function and the diversity of assessment methods present a special challenge for the interpretation of the evidence about the effect of physical activity and exercise on cognitive function.

Does Physical Activity Protect Against the Onset of Age-Related Decline in Cognitive Function or Dementia?

Conclusions

The weight of the available evidence from prospective cohort studies supports the conclusion that physical activity delays the incidence of dementia and the onset cognitive decline associated with aging.

Rationale: Prospective Cohort Studies

At least 17 prospective population-based cohort studies have been published since 1995 that have assessed the association of individuals' level of physical activity with the onset of age-related decline in cognitive functioning among healthy adults or with incident cases of dementia. Studies that confounded the measure of physical activity with other leisure or mental activities were not considered. Four studies showed protective effects against cognitive decline in healthy aging adults (103-106) and two studies did not find protective effects (107;108).

Of the 11 studies of dementia, 7 reported a protective effect of physical activity. Nine of 16 comparisons were statistically significant (mean OR = 0.63 95% CI = 0.50 to 0.80). Though limited in number, results were stronger for Alzheimer's disease than for other dementias, including vascular dementia. Figure G8.8 describes results from prospective cohort studies of physical activity and incident dementia or Alzheimer's disease.

The studies varied considerably in sample size, methods used to assess participant's physical activity level and mental function, and the duration between baseline and follow-up measurements. In general, most studies with sample sizes greater than 1,000 individuals report that physical activity delays the onset of cognitive decline or dementia. The results of studies conducted with smaller numbers of participants are inconsistent. The lack of agreement among the studies reviewed may be explained, at least in part, in terms of statistical power. An alternative explanation for the inconsistencies among the results of these studies is the confounding influence of cognitive stimulation derived while engaged in physical activities (108). In studies that report a relation between physical activity and delayed onset of dementia, the effects were detected using both clinical assessments and standardized measures of cognitive function. Further, early-life (103), mid-life (109), and current levels of physical activity all appear to postpone symptoms of dementia. Thus, although exercise does not prevent dementia, it may be associated with a delay in its onset, perhaps by maintaining a higher level of cognitive function for physically active adults than less physically active individuals as they age (110).

Rationale: Randomized Controlled Trials

A meta-analysis of 18 RCTs (111) indicated that aerobic exercise training produced an effect size (SD) of 0.48 for improving performance on all cognitive tasks, with the greatest effect size (0.68) for executive processing tasks that measure goal-oriented decision-making behavior, compared to 0.46 for controlled-processing tasks that assess attentional effort, 0.42 for visuospatial tasks that evaluate the perceptual organization, and 0.27 for speeded tasks that focus on rapid responses and movements. The results of 2 recently conducted experiments provide support for the facilitative effects of resistance exercise training on information-processing functions of cognitively healthy older adults (85;112), though one experiment found no significant effects of either yoga training or a walking program on older adults' memory or information-processing speed (113).

Figure G8.8 Incident Total Dementia or Alzheimer's Disease: Prospective Cohort Studies, 1995 Through 2007: Crude and Adjusted Hazard

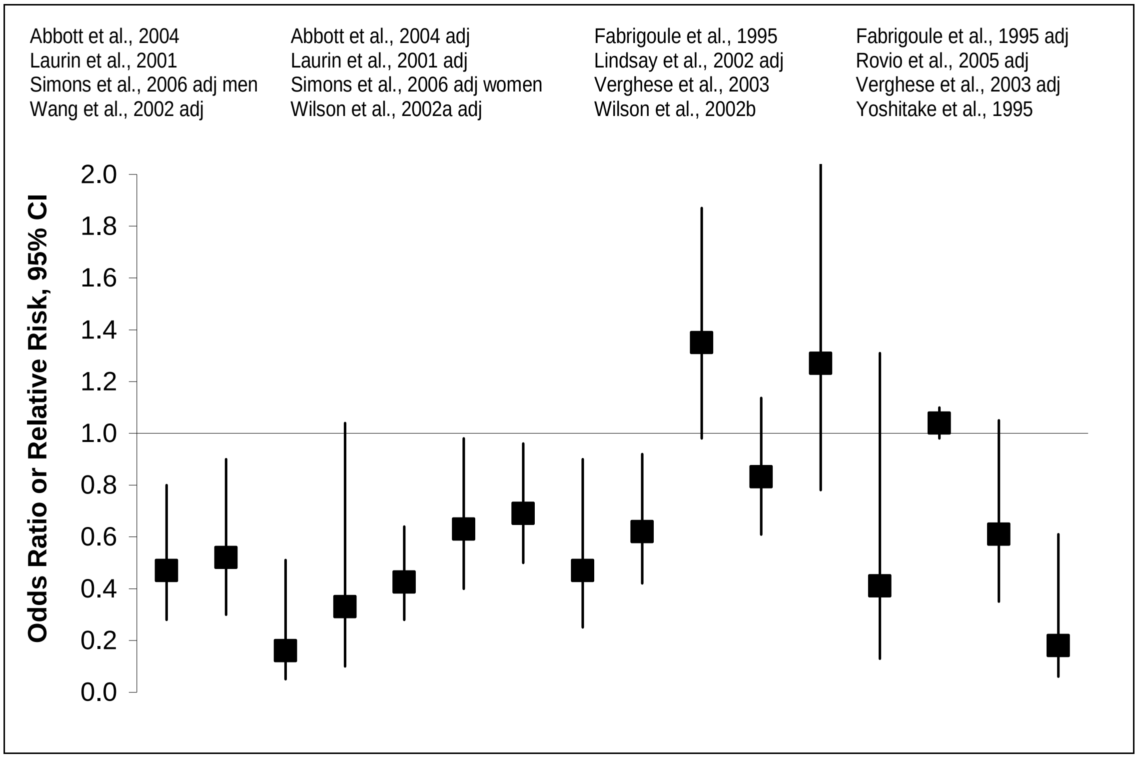

Figure G8.8 Data Points

Author/Date	High	Low	Odds Ratio or Relative Risk
Abbott et al. 2004	0.8	0.28	0.47
Abbott et al. 2004 adj	0.9	0.3	0.52
Fabrigoule et al. 1995	0.51	0.05	0.16
Fabrigoule et al. 1995 adj	1.04	0.1	0.33
Laurin et al. 2001	0.64	0.28	0.425
Laurin et al. 2001 adj	0.98	0.4	0.63
Lindsay et al. 2002 adj	0.96	0.5	0.69
Rovio et al. 2005 adj	0.9	0.25	0.47
Simons et al. 2006 adj men	0.92	0.42	0.62
Simons et al. 2006 adj women	1.87	0.98	1.35
Verghese et al. 2003	1.137	0.609	0.832
Verghese et al. 2003 adj	2.06	0.78	1.27
Wang et al. 2002 adj	1.31	0.13	0.41
Wilson et al. 2002a adj	1.1	0.98	1.04
Wilson et al. 2002b	1.05	0.35	0.61
Yoshitake et al. 1995	0.61	0.06	0.18

Does Physical Activity Reduce Symptoms Associated With Alzheimer's Disease or Other Dementias?

Conclusions

Evidence from RCTs of healthy older adults and people with Alzheimer's disease or other dementias support that regular participation in physical activity improves aspects of cognitive function or reduces symptoms of dementia.

Rationale

A meta-analytic review of 10 randomized controlled studies of older adults diagnosed with cognitive impairments (114) concluded that physical activity interventions benefit the cognitive function of older adults regardless of disease status. Similar to the finding of Colcombe and Kramer (111) with healthy older adults, older adults with impairments who participated in physical activity interventions show better cognitive function than those assigned to control conditions (ES = .57). However, concerns of the methodological integrity of many of the studies reviewed led the authors to recommend caution in the interpretation of these findings. The beneficial effects of physical activity on older adults with dementia have been reported in 2 recent experiments (115;116).

Although individuals with dementia benefit cognitively from participation in exercise training, it is not clear whether physical activity ameliorates symptoms of dementia or simply maintains the level of cognitive function for those who are active. In several experiments, differences in cognitive function and information-processing performance in older adults assigned to physical activity or control conditions was due to the degradation of performance by inactive individuals. Further, although relatively short-term exercise programs demonstrate improvements on older adults' cognitive function, the durability of the effect remains to be determined.

Do the Effects of Physical Activity on Cognitive Function Differ According to Genetics, Age, Sex, Race/Ethnicity, or Medical Condition?

Conclusions

The available evidence supports the benefits of physical activity for improving or maintaining cognitive function among healthy older adults, more so than for young adults whose cognitive health is normally near peak function. The smaller, but generally favorable effects of physical activity on cognitive function and symptoms among people with dementia may be modified by the severity of dementia and other health factors.

Rationale

The protein apolipoprotein E4 (ApoE4) is a known risk factor for Alzheimer's disease. Individuals who have two copies of the ApoE4 allele are at greatest risk for the disease, followed by individuals with one copy of the ApoE4 allele, followed by those who are non-carriers. Investigators have suggested that physical activity diminishes the effects of ApoE4 on the development of Alzheimer's disease. The evidence from prospective cohort studies has been inconsistent, however, with some reporting that physical activity benefits the cognitive functioning of ApoE4 non-carriers and has no effect for ApoE4 carriers (117), and others report that physical activity benefits cognitive functioning for ApoE4 carriers, but has no effect for ApoE4 non-carriers (117;118). Nevertheless, evidence that genetic factors may influence the relation between physical activity and cognition is important as it may help to explain some of the inconsistencies among studies that have examined the effects of physical activity on cognitive performance in the general population of older adults.

The results of one of 15 prospective cohort studies reviewed suggest that sex may modify the relation between physical activity experiences and cognitive function (103). Older Dutch men, but not women, who reported being physical active early in their lives (ages 15 to 25 years) had faster information-processing abilities than those who were less physically active during those years of their lives.

The benefits of physical activity on the cognitive function of older adults who have dementia may be reduced in individuals with cardiovascular risk factors. Daily walking or gardening reduced the 16-year combined risk of Alzheimer's and vascular dementia among elderly male residents of Dubbo, New South Wales in Australia but only daily gardening was protective among females (119). An evaluation of the changes in brain structure and function that accompany Alzheimer's disease and changes in cerebral metabolic processes that accompany ischemia led Eggermont and colleagues (120) to speculate that an individual's cardiovascular risk factors may attenuate or even reverse the positive effects of exercise on cognition and that participation in structured exercise programs may not be beneficial for all patients. Thus, while the bulk of scientific evidence obtained thus far provides compelling support for the benefits of physical activity for healthy older adults, the favorable effects of physical activity may be modified by cardiovascular health or risk. Additionally, the gains in cognitive function brought about by physical activity may be observed more clearly in older adults than young adults, whose level of cognitive health is near its peak and provides less room for exercise-related improvement (121).

Do the Effects of Physical Activity Vary According to Features of Physical Activity, Including Type, Intensity, or Timing (i.e., Session Duration, Weekly Frequency, and Length of Participation)?

Conclusions

Evidence from prospective cohort studies or RCTs is insufficient to determine whether cognitive function or symptoms of dementia vary according to features of physical activity exposure.

Rationale

Four of 6 prospective cohort studies of cognitive decline with aging in healthy people examined more than 2 levels of physical activity exposure. Three of them, including a large cohort of women from the Nurses' Health Study (105), found a dose-response relation, whereby the decline in risk was greater at higher levels of physical activity participation. Four of 10 prospective cohort studies of dementia risk examined more than 2 levels of physical activity exposure. Two of the 4 studies reported a dose-response relation such that higher levels of physical activity result in greater protection against dementia (122;123). The other 2 studies of dementia (124;125) reported similar trends, but the cohorts were too small to detect statistical significance.

The methods used to measure physical activity vary greatly, both among RCTs and prospective cohort studies, which makes it difficult to identify the effects of specific features of physical activity on cognitive function. The use of self-report measures of physical activity is a limitation of prospective studies in general, but it is a unique problem for studies of cognitive function when the measures of physical activity include leisure activities that involve social and cognitive activities but light physical exertion (e.g., crossword puzzles, card games).

Cognitive function has been associated with levels of and gains in cardiorespiratory fitness among healthy, older adults (126-128), and fitness also has been positively correlated with white matter integrity (129), brain volume (130;131), and hippocampal neurogenesis (132). However, the cumulative evidence does not provide clear support that cardiorespiratory fitness is associated with cognitive performance (133).

The sole randomized controlled experiment designed specifically to assess the dose-effect relation between resistance training and information processing in healthy older adults reported that similar benefits were derived from interventions that involved weight loads of either 50% or 80% of maximal strength (85). The results of a large prospective cohort study, led Podewils and colleagues (117) to conclude that, with respect to the onset of dementia, the number of different physical activities in which older adults engage may be more important than their frequency, intensity, or duration. At this time, the dose-response relation among mode, duration, and intensity of exercise training and changes in cognition remains unclear.

Question 5: Is There an Association Between Physical Activity and Sleep?

Introduction

Nearly one-third of the adult population in the United States experiences insomnia every year, and each year 50 to 70 million Americans experience some effects on their health from sleep disorders, sleep deprivation, and excessive daytime sleepiness (134). The financial cost is approximately $65 billion, $50 billion of which represents costs to industry from lost productivity. Approximately 70 sleep disorders exist, the most studied of which are insomnia and obstructive sleep apnea. Many neurological disorders are associated with poor sleep, and poor sleep itself can have important health-related outcomes. Only about 5% to

20% of people who suffer sleep disturbances will seek help from a primary care physician, and many will purchase over-the-counter sleep aids.

Does Physical Activity Protect Against the Onset of Insomnia or Other Sleep Problems?

Conclusions

A small number of observational, population-based studies provides initial evidence supporting a positive association of regular participation in physical activity with lower odds of disrupted or insufficient sleep, including sleep apnea.

Rationale

Population-based studies have found that physically active people report better sleep than inactive people (135), but most of the studies used a cross-sectional design and do not permit conclusions about the temporal sequence of physical activity and sleep. One prospective cohort study (136) found that those who reported more physical activity had nearly 40% lower odds of incident insomnia. Eleven of 13 cross-sectional studies show that the chances of having insufficient or interrupted sleep are lower (mean OR = 0.73 95% CI = 0.66 to 0.81) among adults who are engaged in more physical activity than among those who have less physical activity or are sedentary (136-146). At least 2 population-based, cross-sectional studies found that men and women who exercise at least 3 hours per week had lower odds of sleep apnea measured by polysomnography (147;148). Figure G8.9 shows odds ratios from population-based cross-sectional studies of physical activity and self-ratings of disrupted or insufficient sleep.

Does Physical Activity Reduce Sleep Problems and Enhance Sleep Quality?

Conclusions

The weight of the evidence from a small number of RCTs supports the conclusion that regular participation in physical activity has favorable effects on sleep quality and is a useful component of good sleep hygiene.

Rationale

Six RCTs, all published since 1995, show positive and large effects (more than 1 SD) of exercise training on symptoms of poor sleep and self-rated sleep quality (26;37;149-152). Acute aerobic exercise of varying intensities elicits small to moderate improvements (approximately 4 to 13 minutes) in several features of objectively measured sleep quality, including increases in time spent in slow-wave sleep, total sleep time, and latency for rapid eye movement (REM) sleep, and a decrease in REM sleep among normal sleepers (153). The effects for total sleep time are larger when the exercise lasts more than an hour but do not vary according to people’s fitness levels or the intensity of the exercise. The effects of a

Figure G8.9 Physical Activity and Symptoms of Disrupted or Insufficient Sleep: 13 Cross-Sectional Studies (Total n=84,904)

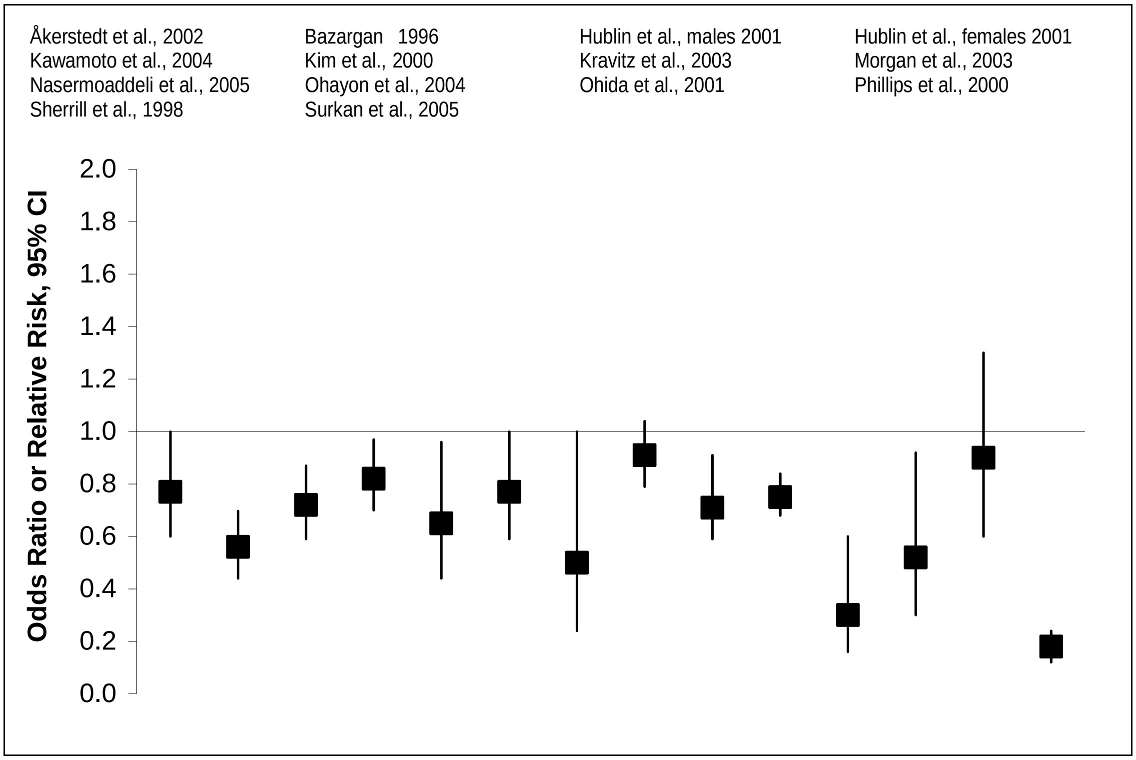

Figure G8.9 Data Points

Author/Date	High	Low	Odds Ratio or Relative Risk
Åkerstedt et al., 2002	1	0.6	0.77
Bazargan 1996	0.697	0.44	0.56
Hublin et al., males 2001	0.87	0.59	0.72
Hublin et al., females 2001	0.97	0.7	0.82
Kawamoto et al., 2004	0.96	0.44	0.65
Kim et al., 2000	1	0.59	0.77
Kravitz et al., 2003	1	0.24	0.5
Morgan et al., 2003	1.04	0.79	0.91
Nasermoaddeli et al., 2005	0.91	0.59	0.71
Ohayon et al., 2004	0.84	0.68	0.75
Ohida et al., 2001	0.6	0.16	0.3
Phillips et al., 2000	0.92	0.3	0.52
Sherrill et al., 1998	1.3	0.6	0.9
Surkan et al., 2005	0.61	0.06	0.18

single exercise session on the sleep of people with sleep disorders are not known. The long-term effects of exercise on objective measures of sleep among poor sleepers have not been studied much (154), and the results of a few RCTs (155-157) and quasi-experimental studies (158;159) of nursing home residents or patients with sleep apnea have been mixed.

Do the Effects of Physical Activity on Sleep Differ According to Age, Sex, Race/Ethnicity, or Medical Condition?

Conclusions

The few RCTs and the scarcity of prospective cohort studies do not permit conclusions about whether the effects of physical activity on sleep differ according to types of people, age, type of sleep disorder, or other medical conditions.

Rationale

Self-reports of exercise frequency and sleep problems were inversely related in a cross-sectional study of a thousand elderly African American residents of New Orleans (138). Older, sedentary adults without cardiovascular disease who complained of sleep problems reported improvements in self-rated sleep after a 16-week exercise program of moderate intensity consisting of 30 to 40 minutes of low-impact aerobics and brisk walking 4 times a week (150). Similarly, older, depressed adults with sleep problems who were not currently being medically treated reported improvements in self-rated sleep that was accompanied by a reduction in depression symptoms (160) after a 10-week, 3-days-per-week, moderately intense (80% of one maximum repetition) resistance training program (26).

Do the Effects of Physical Activity Vary According to Features of Physical Activity Including Type, Intensity, or Timing (i.e., Session Duration, Weekly Frequency, and Length of Participation)?

Conclusions

Evidence from prospective cohort studies or RCTs is insufficient to determine whether features of sleep quality vary according to features of physical activity exposure.

Rationale

In a year-long study of moderate intensity (60% to 85% maximal heart rate) walking or leg cycling exercise (45 minutes or more, 5 or more days each week) among postmenopausal, overweight or obese, sedentary women not taking hormone replacement therapy, morning exercisers who exercised at least 225 minutes per week reported less trouble falling asleep compared with those who exercised less than 180 minutes per week. In contrast, evening exercisers who exercised at least 225 minutes per week reported more trouble falling asleep compared to those who exercised less than 180 minutes per week (152). However, those differences might have been biased, as the timing of exercise sessions were self-selected and most evening exercisers were employed while the morning exercisers were mostly retired or not working. Regardless, increases in cardiorespiratory fitness were related to reduced odds of poor sleep quality, independently of changes in body mass index or time spent outdoors.

Fifteen, 60-minute sessions once a week that emphasized moderate-intensity recreational sports activities (e.g., softball, dance, self-defense, swimming, and athletics) were accompanied by a small increase in self-rating of total time spent sleeping among older, sedentary adults who were group-randomized according to age and socioeconomic status (161). Other studies of less vigorous exercises, such as walking or yoga, have reported smaller or statistically non-significant reductions in self-rated sleep (47;162;163).

Question 6: Is There an Association Between Physical Activity and Other Aspects of Mental Health?

Introduction

Physical activity and exercise may have the potential to reduce the onset or progression of central nervous system disorders other than dementia that contribute to disability and mortality risk, such as multiple sclerosis (164) and Parkinson's disease (165). They also may reduce the adverse impact of these disorders on quality of life. However, too few prospective cohort studies and RCTs have been conducted to allow conclusions about the protective effects of physical activity for CNS diseases other than Alzheimer's disease and other dementias.

Benefits of physical activity may also extend to other aspects of mental health that are less directly linked to disability and mortality risks but are important contributors to overall quality of life, such as self-esteem and feelings of energy/fatigue. Sufficient evidence exists to encourage more study in these areas, but presently not enough studies are available to draw conclusions about how the effects of physical activity or exercise might differ according to types of people or types and amounts of physical activity.

Self-Esteem

Enhanced self-esteem has significance for mental health because it conveys a feeling of value or self-worth and it is a generalized indicator of psychological adjustment and health risk (89). A meta-analysis of about 50, mostly small, RCTs of various types of exercise reported an average increase in self-esteem of about 0.25 SD among adults (166). Self-esteem is increased among adults (166) when physical fitness is increased. However, because features of physical activity exposure were not associated with self-esteem outcomes in the studies, it is difficult to conclude that fitness influences self-esteem independently of other diverse aspects of the studies' methods, social contexts, and participant expectations of benefit. Nonetheless, larger gains in self-esteem can be expected for individuals with low initial levels, and for whom physical attributes have a relatively high value as a part of global self-concept.

Chronic Fatigue

The literature on physical activity and chronic fatigue syndrome is small, and epidemiologic studies of this condition rarely have included measures of physical activity. Five relatively small RCTs all show a positive effect of exercise training on symptoms of chronic fatigue syndrome (167-171). A dozen population-based observational studies, including 4 prospective cohorts published since 1995, suggest a protective effect of physical activity against feelings of fatigue or low energy (OR = 0.61, 95% CI = 0.52 to 0.72) (172), and RCTs of groups of medical patients and other adults show a moderate reduction in symptoms of fatigue (173;174).

Question 7: Is There an Association Between Physical Activity and Adverse Psychological Events?

Some adverse psychological events have been reported among extremely active people, but whether they are causally influenced by physical activity exposure is not yet known. Clinical cases of "running addiction," were described 30 years ago (175), whereby motivation for running exceeded commitments to work, family, social relations, and medical advice. Similar cases have been labeled *positive addiction, runner's gluttony, fitness fanaticism, athlete's neurosis, obligatory running*, and *exercise abuse*.

However, little is understood about the origins, valid diagnosis, or mental health impact of exercise abuse (176;177). Though exercise abuse or addiction is a recognized problem for clinical medicine, its population prevalence is unknown but likely low. Likewise, it is not known whether excessive exercise and disordered eating share a common course that is motivated by common goals and followed by common medical outcomes. It has been proposed that anorexia athletica is a subclinical syndrome of anorexia nervosa (178), but the prevalence of disordered eating and the independent risk caused by sport and exercise have not yet been established by controlled epidemiologic and clinical studies. In most cases, the eating behaviors of athletes do not appear to signal anorexia nervosa or bulimia (i.e., bingeing and purging (179)), which have prevalence rates in the United States of about 1% and 4%, respectively. Cases of muscle dysmorphia, a proposed form of body dysmorphic disorder, in which a person develops a pathological preoccupation with his or her muscularity and has associated symptoms of severe subjective distress, impaired social and occupational functioning, and abuse of anabolic steroids and other substances, have been reported (180;181). No population-based studies have been conducted to determine the prevalence of muscle dysmorphia nor any prospective cohort studies or randomized clinical studies to determine whether muscle dysmorphia or body dysmorphia results from participation in resistance exercise training or whether people who have existing vulnerability to a distorted body image and self-concept are drawn to weightlifting.

Results from nearly 100 studies on these potential adverse events of participation in exercise training and sports are inconclusive because the studies described symptoms among different groups of active or inactive people without fully considering attributes other than activity history that might account for abusive exercise or eating problems (177). Risk profiles of exercise abusers or athletes have not been evaluated against those of non-athletes from the same academic, socioeconomic, or psychological backgrounds. The studies often lack standard definitions or valid measures of physical activity or disordered eating. Though anorexics often augment food restriction by hyperactivity, their aerobic fitness is well below average because of muscle wasting and anemia, in contrast to the above-average aerobic fitness of habitual runners and trained athletes. In addition, cross-sectional studies have not revealed a common psychopathology between obligatory (i.e., excessively committed) runners and anorexic patients.

Anxiety can be elevated slightly immediately after maximal exercise testing or heavy resistance exercise (i.e., approximately 80% of 1 repetition maximum (182;183)), but that elevation is temporary. Nonetheless, overall reductions in anxiety can be delayed by 1 or 2 hours after resistance exercise is completed. Evidence from 15 studies refutes the potential association between exercise and panic attacks; only 5 panic attacks were reported during exercise involving 444 exercise bouts performed by 420 panic disorder patients (184). Research has also shown that lactate accumulation resulting from exercise is not related to increased risk of panic attacks among patients with panic disorder (185) or postexercise anxiety in normal individuals (186). Moreover, a small, randomized clinical trial recently showed that 10 weeks of aerobic exercise training was effective in reducing symptoms of anxiety among patients with panic disorder and agoraphobia (72).

Question 8: What Mechanisms Can Plausibly Explain the Association Between Physical Activity and Mental Health?

Very limited evidence exists about biological mechanisms that can explain the effects of physical activity or exercise on mental health (187). It is accepted that the brain and the rest of the central nervous system regulate moods, emotions, cognitions, sleep, and neurological functions, and that social and environmental factors interact with genes to regulate the brain. Experimental animal studies show that both voluntary and forced running activate and produce adaptations in several aspects of brain neural circuits involved with learning, memory, motivation, and behaviors that mimic features of human depression, anxiety, and cognitive function. These include neurotransmitters (e.g., acetylcholine, glutamate, and gamma-aminobutyric acid), neuromodulators (e.g., dopamine, norepinephrine, and serotonin) and their receptors, neuropeptides that influence neurotransmission (e.g., galanin and neuropeptide Y), and neuronal growth factors (e.g., brain derived neurotrophic factor and VGF), all of which are targets of experimental treatments for depression and anxiety. However, only a few studies have used animal models of mental or neurological disorders, testing whether brain and behavior changes coincide as predicted after physical activity (e.g., 188-194). Likewise, the way in which exercise regulates sleep has received little study and is unknown. Indirect evidence suggests that acute bouts of exercise are positively associated with melatonin production in women (195) and can induce circadian phase shifts (196) including a phase delay in circadian melatonin rhythm (197), influence adenosine metabolism (198), and activate brain neurological circuits hypothesized to help people feel less anxious and depressed (154).

Unlike other chronic diseases, non-biological mechanisms also may explain the effect of physical activity on mental health. Cognitive explanations include increased self-esteem (e.g., 199), perceptions of social support, and efficacy beliefs about personal control. Similarly, acute responses to single exposures of physical activity, such as transient changes in moods (200;201) or feelings of energy; pleasant (e.g., enjoyment) or unpleasant (e.g., discomfort or pain) affective experiences during exercise; or nightly sleep (153), are likely to contribute to the accumulative psychological responses that typically are measured only after chronic exposure to physical activity. Also such responses might contribute indirectly by increasing exposure to physical activity (e.g. better adherence to exercise) or by influencing other factors important to mental health (e.g., social engagement). Tests of those contributions will require research designs and methodologies that are difficult to implement with tight control in clinical or public health settings (e.g., 202-206). Thus, continued experimental research on biological mechanisms and innovative tests of social or cognitive mediators of psychological responses are needed to confirm and explain the evidence from prospective observational studies and RCTs that physical activity and exercise promote mental health.

Overall Summary and Conclusions

The weight of the cumulative evidence from prospective cohort studies and RCTs of uneven quality supports the conclusion that physical activity has protective benefits for several aspects of mental health. The evidence is strongest for protection against symptoms of depression and cognitive decline associated with aging, including the onset of dementia. Substantial evidence also suggests that physical activity reduces symptoms of anxiety and poor sleep, as well as feelings of distress and fatigue, and enhances well-being. Physical activity generally appears equally beneficial for adults regardless of age, sex, race/ethnicity, or health status, but few studies have directly compared benefits or hazards of physical activity among those population segments. Minority groups have been poorly represented in most studies. A small number of prospective cohort studies suggest that health benefits for depression and dementia are greater with higher levels of physical activity exposure, but insufficient evidence precludes conclusions about the minimal or optimal types or amounts of physical activity for mental health. Benefits do not appear to depend on fitness or fitness gains. Current evidence supports the conclusion that regular participation in moderate-to-vigorous physical activity, consistent with current public health guidelines, confers mental health benefits when compared to participation in low levels of physical activity or a sedentary lifestyle.

Research Needs

This review of physical activity and mental health identified a number of research needs. First, more prospective cohort studies and tightly controlled RCTs are needed, especially for anxiety and sleep disorders. Specifically:

- More studies of under-represented groups and of people at high risk of mental health disorders are needed.
- Selection of potential confounders specific to mental health risks need to be included in prospective cohort studies.
- Reporting of adherence to and dropout from trials should be improved, particularly with respect to the impact on the trial's efficacy and likely population effectiveness.
- Investigators should strive for convergence of subjective and objective measures of physical activity and should specify the social and environmental contexts in which physical activity occurs.
- Valid outcome measures need to be selected, refined, and used uniformly.
- Physical activity exposures and outcomes need to be measured frequently to permit investigators to model change.
- It would be helpful to conduct additional RCTs comparing the effects of exercise with other preventive interventions.
- Novel designs that distinguish social moderators and mediators of outcomes from experimental contamination (i.e., placebo effects) would make a valuable contribution to the field.

A second important research need is studies that manipulate or directly compare standardized features of physical activity, including type, intensity, and timing, with the settings in which activity takes place (e.g., group vs. solitary, community vs. home, indoor vs. outdoor).

Finally, it would be helpful to accelerate the synergy between human brain imaging studies and neuroscience studies that use animal models of human disease. This improved synergy could help elucidate biological mechanisms underlying the benefits of physical activity to mental health. An increased emphasis on modeling of social-cognitive mediators of mental health outcomes and studies of gene-environment interactions also would be valuable additions to the field.

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Part G. Section 9: Youth

Introduction

Physical activity in American children and adolescents has been a concern of authorities in education, medicine and public health for more than half a century. During most of this period, experts have focused on physical fitness rather than physical activity, per se. During the post-World War II era, concerns about military preparedness led to formation of the President's Council on Physical Fitness and Sports. The Council initiated a youth physical fitness testing program that was intended to promote participation in fitness-enhancing physical activity in children and adolescents. In association with that fitness testing program and others, standards for physical fitness in young people have been developed.

Although these standards for physical fitness in youth have been available for many years, only in the past decade have professional and scientific organizations presented guidelines for physical activity in children and youth. Different groups have taken various approaches to the task of identifying recommended levels of physical activity for young persons. Some expert panels have approached this task by focusing on the health effects of controlled exercise training in youth. Other groups have considered cross-sectional and longitudinal associations between physical activity and various health-related factors.

The task of relating physical activity to indicators of health and fitness is complex. Part of the complexity relates to 3 processes that are ongoing during the first 2 decades of life: normal physical growth, biological maturation, and behavioral development. These processes occur simultaneously and interact, especially during adolescence, making their individual and combined effects difficult to evaluate. Physical activity, a behavior that has its own developmental pattern, is only one of many factors that may influence indicators of health and fitness in youth. It may be difficult to partition effects attributed to physical activity from those associated with normal growth, maturation, and development.

Review of the Science

Overview of Questions Addressed

This chapter addresses key questions related to the relation between physical activity and a select number of health-related outcomes in children and adolescents. These outcomes are physical fitness, body composition, cardiovascular and metabolic disease risk factors, bone health, and mental health. For each of the selected health outcomes, the committee considered the following questions:

1. Is there a significant relation between physical activity and the outcome?
2. If so, has a dose-response pattern been established?
3. If a relation is evident, is it influenced by age, developmental status, sex, race/ethnicity, and/or socioeconomic status?

Data Sources and Process Used to Answer the Questions

The Youth subcommittee decided to apply 3 important delimitations in performing the review of scientific literature summarized here. First, the review was limited to studies of school-aged children aged 5 to 19 years. Although it certainly would be relevant to consider studies of younger children, it was the subcommittee's judgment that the scientific literature on physical activity and health is too limited in infants and preschool-age children to support clear conclusions.

Second, the subcommittee opted to focus its review on the relation between physical activity and the modest number of health-related outcomes noted above. Third, the subcommittee focused on the effects of physical activity on health outcomes as observed **during childhood and adolescence.** The subcommittee recognized the significance of the potential long-term effects of physical activity during childhood and adolescence on health outcomes later in life. It also was concerned about the potential influence of physical activity early in life with physical activity in adulthood. However, the subcommittee judged that the scientific literature pertinent to the latter 2 relationships is currently insufficient to inform physical activity guidelines. Hence, the review presented in this chapter is limited to an examination of the relation between physical activity and selected health-related outcomes during childhood and adolescence.

For each of the aforementioned health-related outcomes, the subcommittee performed a systematic evidence-based review of the literature using the *Physical Activity Guidelines for Americans* Scientific Database as its primary resource (see ***Part F. Scientific Literature Search Methodology***, for a detailed description of the Database). The review consisted of publications from 1995 onward, with the exception of some review papers on cardiorespiratory fitness. This was due to the fact that many studies on the effects of endurance training on cardiorespiratory fitness were published before 1995. The subcommittee examined reviews, meta-analyses, randomized controlled trials (RCTs), non-randomized controlled trials, prospective cohort studies, cross-sectional studies, and additional observational studies. As needed, the subcommittee also used systematic reviews, meta-analyses, and original studies from sources other than the Scientific Database.

Question 1: Is Physical Activity Significantly Related to Cardiorespiratory Fitness Among Children and Adolescents? If So, Is There an Established Dose-Response Pattern? Is the Relation Influenced by Age, Developmental Status, Sex, Race/Ethnicity, or Socioeconomic Status?

Conclusions on Relation and Dose-Response Pattern

Physical activity is positively related to cardiorespiratory fitness in children and youth, and both preadolescents and adolescents can achieve improvements in cardiorespiratory fitness with exercise training. Endurance training has been shown to increase VO_{2max} by 5% to 15%. Due to variability across studies, the optimal dose of physical activity needed to attain improvements in cardiorespiratory fitness cannot be specified (1;2). In a recent review, Baquet and colleagues (3) summarized the dose of exercise prescribed across 22 controlled training studies. They concluded that an intensity greater than 80% of maximal heart rate, a frequency of 3 to 4 days per week, a duration of 30 to 60 minutes per session, and a length of 1 to 3 months resulted in improvements in cardiorespiratory fitness (3).

Rationale for Relation and Dose-Response Pattern

This review of the literature was based on an evaluation of 2 review articles, 1 meta-analysis, 10 cross-sectional studies (Table G9.A1, which summarizes these cross-sectional studies can be found at http://www.health.gov/paguidelines/report/), 1 prospective cohort study, and 21 experimental studies. The experimental studies can be further classified as randomized trials (n=6), group randomized trials (n=3), non-randomized trials (n=8), before and after studies (n=2), and time series studies (n=2) (Table G9.A2, which summarizes these experimental studies, can be accessed at http://www.health.gov/paguidelines/report/). Typically, most cross-sectional studies either correlated cardiorespiratory fitness with physical activity levels or compared active youth to inactive youth. Cardiorespiratory fitness was assessed with a variety of methods, including step test, cycle ergometer, 20-meter shuttle run, and treadmill test. All of the studies reported an association between physical activity and cardiorespiratory fitness. In particular, Ara and colleagues (4) reported that males who participated in 3 hours of extracurricular physical activities per week in addition to regular physical education classes had significantly greater aerobic fitness compared to males who participated only in regular physical education classes. In another study, Dollman and colleagues (5) measured both sedentary behavior and moderate to vigorous physical activity. They reported that males who watched television for more than 2 hours per day and engaged in more than 60 minutes of moderate to vigorous physical activity (MVPA) had higher cardiorespiratory fitness compared to males who watched television for more than 2 hours per day but obtained less than 60 minutes of MVPA (5). Females who engaged in more than 60 minutes of MVPA (regardless of their television viewing habits) had greater cardiorespiratory fitness levels than females who obtained less than 60 minutes of MVPA (5). In all of the remaining cross-sectional studies, the dose of physical activity was not provided. Overall, cross-sectional studies concluded that youth with higher physical activity levels tended to have higher cardiorespiratory fitness levels.

In the only prospective cohort study that met the search criteria, Ara and colleagues (6) assessed physical activity in 42 boys with an average age of 9 years, and followed them for 3 years. The boys were divided into a physical activity group (participating in at least 3 hours of extracurricular physical activities per week plus regular physical education classes) and a non-physical activity group (participating only in regular physical education classes) (6). Cardiorespiratory fitness was assessed with the 20-meter shuttle run test. At the conclusion of the 3-year period, the physical activity group maintained their cardiorespiratory fitness levels, whereas the non-physical activity group decreased their cardiorespiratory fitness levels (6).

Most of the 21 experimental studies reported increases in cardiorespiratory fitness in a range from 5% to 15% with endurance training. The most common activities were aerobics, running, cycling, using exercise machines, stair climbing, basketball, and brisk walking. The dose of endurance training varied across studies. Frequency ranged from 1 to 5 days per week, duration was between 20 and 60 minutes per session, and intensity ranged from 70% to 90% of maximum heart rate (HRmax).

Conclusions on Developmental and Demographic Influences

Both children and adolescents can increase their cardiorespiratory fitness with endurance training, and males and females respond similarly to endurance training. The literature is not adequate to support a conclusion regarding race/ethnicity. Most studies did not report the socioeconomic status of participants, thereby precluding conclusions about the influence of this demographic factor.

Rationale for Developmental and Demographic Influences

Age and/or Developmental Status

Children and adolescents can achieve improvements in cardiorespiratory fitness with physical activity. Twenty-one experimental studies examining this relation have included subjects who range in age from 5 to 18 years. In all but one study (7), physical activity produced improvements in cardiorespiratory fitness, whether preadolescents, adolescents, or both were active.

Sex

Both males and females have demonstrated their capacity to attain similar improvements, ranging from 5% to 15%, in cardiorespiratory fitness as a result of endurance training (1;2;8-12).

Race/Ethnicity

Information about the potential influence of race/ethnicity on cardiorespiratory fitness in youth is limited. Most studies have focused on white children and adolescents, but of the 4 studies that examined the effect of endurance training on cardiorespiratory fitness in African American youth, all found significant improvements in cardiorespiratory fitness of 5% to 10% (8;10;13;14). Crews and colleagues (15) implemented a 12-week intervention among Hispanic children, and reported significant improvements (16%) in cardiorespiratory fitness.

Socioeconomic Status

Most studies did not report the socioeconomic status of participants, thereby preventing conclusions about the influence of this factor on physical activity and cardiorespiratory fitness.

Question 2: Is Physical Activity Significantly Related to Muscular Strength Among Children and Adolescents? If So, Is There an Established Dose-Response Pattern? Is the Relation Influenced by Age, Developmental Status, Sex, Race/Ethnicity, or Socioeconomic Status?

Conclusions on Relation and Dose-Response Pattern

Physical activity is positively related to muscular strength. In both children and adolescents, resistance training 2 or 3 times per week significantly improves muscular strength.

Rationale for Relation and Dose-Response Pattern

A total of 5 review articles and 2 non-randomized trials were included in this evaluation of the evidence. Malina (16) reviewed 22 experimental studies of pre- and early-pubertal youth and muscular strength training programs and reported a significant increase in muscular strength. Most of the resistance training programs were 8- or 12-week programs that consisted of 2- and 3-day sessions separated by days of rest; the range of all reviewed programs was 6 weeks to 21 months. Less than half of the studies reported intensities, but of those that did, training intensities ranged from 50% to 85% of 1 repetition maximum (1RM), with 75% 1RM being the most common. Conversely, when participants stopped the resistance training (detrained), they experienced a decrease in muscular strength. Growth and maturation were taken into account in this review, and Malina concluded that resistance training did not have a negative effect on these developmental factors among pre- and early-pubertal youth.

Blimkie and Bar-Or (17) reviewed 18 studies of adolescents and concluded that moderate to high training loads resulted in significant increases in muscular strength. However, Blimkie and Bar-Or also noted that for both preadolescents and adolescents, “the optimal combination of mode, intensity, volume and duration of training for strength increases…has yet to be determined" (p.115). Other review articles reported increases in muscular strength with resistance training among prepubertal children (18-20).

Treuth and colleagues (21) implemented a non-randomized resistance training study in a sample of obese girls aged 7 to 10 years. Over a period of 5 months, the girls trained with 6 upper body and 1 lower body exercises for 3 days per week, 20 minutes per session. The sequence of exercises for each session was leg press, bench press, military press, bicep curl, latissimus pull down, triceps extension, and sit-ups. Each participant performed 2 sets of 12 repetitions for the upper body exercises and 2 sets of 15 repetitions for the leg press. Weight was gradually increased throughout the program to 70% 1RM. At the conclusion of the trial, the intervention group significantly increased their 1RM bench press by 19.6%, 1RM leg press by 20%, and knee extensor strength by 35%.

Faigenbaum and colleagues (22) studied the effects of a 9-week non-randomized progressive resistance training study in boys aged 13 years. The program consisted of resistance training exercises 2 days per week for 90 minutes per session. A typical training session began with a 10-minute warm-up, followed by 2 or 3 types of Olympic-style lifts and then a series of resistance exercises: barbell squat, leg curl, bench press, front latissimus pull down, seated row, biceps curl, and triceps extension. For each exercise, 3 sets were performed, with 1 to 4 repetitions for the Olympic-style lifts per set, and with 12 to 15 repetitions decreasing to 8 to 10 repetitions for the resistance exercises per set. The program increased leg strength by 19% and upper body strength by 15%.

Conclusions on Developmental and Demographic Influences

Both children and adolescents can increase their muscular strength with resistance training, and males and females show similar relative increases in strength with resistance training. The literature is too limited to support conclusions about the influence of race/ethnicity and socioeconomic status.

Rationale for Developmental and Demographic Influences

Age and/or Developmental Status

Children, pre- and early-adolescents can improve their muscular strength with resistance training (16;18-20). In addition, resistance training does not have adverse effects on growth and maturation (16).

Sex

Both males and females can obtain increases in muscular strength with resistance training (21;22), although approximately half of the studies reviewed by Malina (16) were of males only.

Race/Ethnicity

Information about the potential influence of race/ethnicity on muscular strength is limited. Most studies have been conducted with white children and adolescents.

Socioeconomic Status

Most studies did not report the socioeconomic status of participants, thereby preventing conclusions about the influence of socioeconomic status on muscular strength.

Question 3: Is Physical Activity Significantly Related to Body Composition in Children and Adolescents? If So, Is There an Established Dose-Response Pattern? Is the Relation Influenced by Age, Developmental Status, Sex, Race/Ethnicity, or Socioeconomic Status?

Conclusions on Relation and Dose-Response Pattern

Among normal-weight youth, those who have relatively high levels of physical activity tend to have less adiposity than youth with low levels of physical activity. However, programs that increase physical activity in normal-weight youth typically have little effect on adiposity.

Controlled training studies with overweight/obese youth have observed reductions in overall adiposity and visceral adiposity with exposure to regular physical activity of moderate to vigorous intensity 3 to 5 times per week, for 30 to 60 minutes. The most consistent favorable effects of physical activity on adiposity were found in studies that used dual-energy x-ray absorptiometry (DXA) to estimate percent body fat and magnetic resonance imaging to estimate visceral adipose tissue (VAT), in contrast to studies based on body mass index (BMI) or skinfold estimates of percent body fat based on skinfold thicknesses. Evidence for a dose-response pattern is inconsistent in the studies reviewed.

Rationale for Relation and Dose-Response Pattern

Caveats

Indicators of body composition change with chronological age (CA) and associated changes in normal growth and maturation (18). As a result, it is difficult to partition physical activity effects from those expected with growth and maturation. On average, BMI declines during infancy and early childhood, reaches a nadir at about 5 to 7 years, and then increases through the remainder of childhood and adolescence. The timing of the increase is labeled the “adiposity rebound.” Fat-free mass (FFM) shows a growth pattern similar to that of height, with a major adolescent spurt; fat mass (FM) increases, on average, consistently with age. Percent fat (%F) increases during childhood but declines during adolescence in males and continues to increase at a slower pace in females during adolescence. Sex differences are negligible in BMI; they are small in FFM and FM during childhood and increase during adolescence (FFM males larger, FM females larger). The sex difference in %F (greater in females than males) is consistent from childhood through adolescence.

Indicators of body composition are also related to biological maturity status. On average, among youth of the same CA, those advanced in maturity status are larger in size, BMI, FFM, and FM compared to those "on time" or delayed in maturity status. With the exception of pubertal status, only one of the studies reviewed included age at peak height velocity (PHV) as a maturity indicator, while no studies incorporated skeletal age. Many studies included an estimate of pubertal status, either clinically assessed or self-reported stage of breast or pubic hair in girls, or genital or pubic hair in boys; menarcheal status is occasionally considered. Stages of breast and pubic hair and genital and pubic hair are not equivalent in girls and boys, respectively. Pubertal status so estimated simply means that the youth was in a particular stage; it provides no information about when the youth entered the stage or how long he or she had been in a stage. Further, pre-pubertal children (no overt signs of puberty) of the same CA can vary up to 3 to 4 years in skeletal age.

As an indicator of adiposity, BMI has limitations when evaluating the influence of physical activity in intervention studies. In normal-weight children, BMI is about equally correlated with FFM and FM and %F; it is a better indicator of overall body size (weight-for-height), not necessarily adiposity. In overweight and obese youth, BMI may be more highly correlated with %F, although some overweight or obese youth also have a large FFM. Activity may alter body composition without a change in BMI. In addition, BMI may have different meanings among ethnic groups, given well-established ethnic variation in body proportions (especially relative leg length and, by inference, relative upper limb length).

Measurement variability may be a factor in looking at changes in skinfolds with intervention training studies. In the studies reviewed, the change attributed to physical activity may be within the range of measurement error. Also, the standard error of estimation (SEE) of %F prediction equations from skinfolds is not considered; SEEs are in the range of 3-5%. A number of more recent studies use DXA, which should improve the precision of body composition estimates.

Evidence

This review of the evidence is based on an evaluation of 45 cross-sectional studies (Table G9.A3, which summarizes these cross-sectional studies, can be accessed at http://www.health.gov/paguidelines/report/), 21 prospective cohort studies, 21 experimental studies in normal-weight children and adolescents, and 16 training studies in the overweight and/or obese. The 37 training studies can be further classified as 13 randomized trials, 9 group randomized trials, 12 non-randomized trials, and 3 before-and-after studies. Study participants ranged in age from 3 to 18 years, and a variety of indicators of physical activity was used.

Cross-Sectional Studies

The majority of studies used correlation and regression, and samples were of mixed weight status (normal-weight, overweight, obese). Across studies, physical activity has a low and, at best, moderate relation with BMI, percent body fat, fat mass, and skinfold thicknesses. The correlations are reasonably consistent across studies considering the mix of methods used to measure and estimate physical activity. The magnitude of correlations and regression estimates indicates that physical activity accounts for a relatively small percentage of the variance in BMI and indicators of adiposity, and that other factors explain most of the variance. Nevertheless, youth who engage in more physical activity, specifically vigorous physical activity, tend to have less adiposity than those who engage in less physical activity (4;23-25).

Several analyses of cross-sectional data have suggested a number of steps per day and energy expenditure or physical activity that are necessary for maintaining normal weight in youth. Recommended cut-off points for normal weight children are 12,000 and 15,000 steps per day for girls and boys aged 6 to 12 years, respectively (26), and 13,000 and 16,000 steps per day for girls and boys aged 5 to 12 years, respectively (27). An association between 60 minutes per day of physical activity with an energy expenditure of 8 or more kcal/kg/day and acceptable levels of BMI and percent body fat also has been noted in youth aged 9-11 years (28).

Prospective Cohort Studies

The prospective cohort studies are of mixed designs and are at times difficult to interpret (Table G9.A4, which summarizes these prospective cohort studies, can be accessed at http://www.health.gov/paguidelines/report/). Several trends are apparent, however:

- The school-based CATCH intervention had no effect on BMI and skinfolds (29;30).
- The Nurses' Health Study II offspring showed smaller than expected estimated changes in BMI associated with physical activity, although the association may be of clinical relevance if the effects are cumulative (31;32).
- One study suggested that active children may have a later adiposity rebound than less active children, though it is not clear in the study whether the rebound was modeled in individual children (33).
- One study considered changes relative to estimated age at peak height velocity, with the results suggesting that an increase in physical activity may control the accrual of fat mass from childhood through adolescence in males (34).
- Other studies generally show a small relation between physical activity levels and changes in indicators of adiposity or mixed results.

Experimental Studies in Children of Normal Weight or Mixed Weight Status

With few exceptions, experimental studies show a small increase in BMI and adiposity indicators, or no significant changes in the BMI and adiposity indicators with training (Table G9.A5, which summarizes these experimental studies, can be accessed at http://www.health.gov/paguidelines/report/). Training protocols varied among studies, but the majority focused on relatively continuous activity, primarily endurance activities. Durations of protocols also varied — less than 10 weeks (6 studies); 10 to 15 weeks (8 studies); 16 to 20 weeks (2 studies); longer than 20 weeks (7 studies) — but results do not appear to vary with protocol duration. Of the studies with durations longer than 20 weeks, results were mixed. A 10-month intervention of continuous activity (35) showed a significant reduction in percent body fat, but a 10-month intervention of brief high-impact physical activity (36) showed no effect on weight and fat mass. Results were similar when the brief high-impact physical activity intervention was extended over 2 years (37). Two interventions that extended over 1 school year had different results, with Schneider and colleagues (38) showing no effect of physical activity on percent body fat and Viskic and colleagues (39) showing a larger decrease in percent body fat in the experimental compared to the control group. One study over 2 school years showed a smaller gain in BMI in an intervention group that included parental support compared to a control group and an intervention group without parental support (40). An even longer study, which extended over 3 to 4 years, showed no influence of added physical education on fat mass (41).

Two studies (35;42;43) were conducted in which investigators did not specifically choose youth who were overweight or obese to participate. However, the youth who chose to participate had mean baseline BMIs that met the International Obesity Task Force criteria for overweight. The studies used a relatively large dose of moderate to vigorous physical activity (80 minutes per day, 5 days per week for 8 months (42) and 10 months (35)) and noted a small but significant reduction in percent body fat. Youth with better attendance had a larger decline in percent body fat (43) and a smaller increase in BMI (35) over the course of the study.

Experimental Studies in Overweight or Obese Children

Results among studies are somewhat variable, but most suggest a decline in BMI and percent body fat in overweight or obese youth with training, though there are several exceptions (Table G9.A6, which summarizes these experimental studies, can be accessed at http://www.health.gov/paguidelines/report/). The most consistent results for percent body fat and visceral adipose tissue are Gutin and colleagues (8;35;42-46). Most studies use continuous, largely aerobic activity, 3 to 5 times per week for 30 to 60 minutes. Durations vary: 8 weeks (1 study); 10 weeks (1 study); 12 weeks (4 studies); 3 to 5 months (4 studies); 6 to 10 months (4 studies). Two studies of strength training show minimal effects on adiposity in obese youth (21;47).

Conclusions on Developmental and Demographic Influences

Variations in the effects of physical activity on adiposity associated with age, sex, biological maturity status, race/ethnicity, and socioeconomic status have not been systematically considered in the literature. Studies are variable in controlling for the potential influence of age per se and maturity status in the respective analyses. No conclusions regarding the effects of age and maturity can be made at this time.

Question 4: Is Physical Activity Significantly Related to Cardiovascular and Metabolic Health in Children and Adolescents? If So, Is There an Established Dose-Response Pattern? Is the Relation Influenced by Age, Developmental Status, Sex, Race/Ethnicity, or Socioeconomic Status?

Conclusions on Relation and Dose-Response Pattern

Physical activity is positively related to cardiovascular and metabolic health in youth. A dose-response relation appears to exist, in that greater doses of physical activity are associated with higher levels of cardiovascular and metabolic health. However, the precise pattern of the dose-response relation has not yet been determined.

Rationale for Relation and Dose-Response Pattern

To examine the relation between physical activity and cardiovascular and metabolic health, a total of 43 studies were considered: 21 experimental studies, 2 prospective cohort studies, and 20 cross-sectional studies. Of the 21 experimental studies, 13 were randomized trials, 2 were group randomized trials, 2 were non-randomized trials, 2 were time series studies, 1 was a before-and-after study, and 1 was another type of study that included a comparison group.

Physical activity may exert much of its influence on cardiovascular and metabolic health by enhancing fitness and reducing fatness, which in turn influence the underlying processes leading to cardiovascular disease and type 2 diabetes. Thus, studies typically have focused on risk factors for these two diseases, namely fasting levels of insulin, lipids, and inflammatory markers. Some recent studies have gone further to determine whether physical activity influences mechanisms, such as cardiac parasympathetic activity, and end-organ parameters, such as endothelial function, left ventricular (LV) geometry and function, arterial stiffness, and carotid intima-media thickness (IMT). Because so little information is currently available on these variables, and because of the interrelations among them and the cardiovascular disease/type 2 diabetes risk factors, we have tried to draw generalizations across the entire risk profile.

Observational studies have reported that youth who engage in relatively large amounts of physical activity have more favorable risk profiles than youth who engage in relatively little physical activity (48-56). Because RCTs have shown that physical activity decreases total body and visceral fatness (35;45;46), which are themselves related to poor risk status (57), it is noteworthy that, to some degree, the association of physical activity to favorable risk profile is retained even after controlling for the possible mediating effect of body fatness (58-62). Some evidence indicates that the relation of physical activity to improved insulin sensitivity is clearer in boys than in girls (63). Evidence also suggests that the relation between level of physical activity and lipids and lipoproteins is primarily with triglycerides and HDL-cholesterol; physical activity has little influence on LDL-cholesterol. However, in children with elevated LDL-cholesterol, increased levels of physical activity may be associated with a prospective trend to lower LDL-cholesterol (64).

In recent years, a metabolic syndrome underlying cardiovascular disease and type 2 diabetes has been identified in adults, and the concept of risk factor clustering as being especially detrimental has been extended to youth (65). When investigators have derived clustering scores, they have found that youth who engaged in more physical activity had better scores than did inactive youth (53).

Investigations of physical activity and risk profiles have generally focused on aerobic physical activity. However, some evidence is available that youth with substantial muscle strength, as a proxy for strength-building physical activity, have good insulin sensitivity (66). This subject deserves further study.

Taken together, the observational results support the hypothesis that physical activity is associated with a favorable risk profile. A number of studies have tested this hypothesis using controlled interventions. Because of the potential role of fatness as a mediator of the relation between physical activity and risk profile, many RCTs have used subjects who were obese at baseline.

The information available from such intervention trials in obese youth suggests that controlled physical activity programs lasting 2 to 8 months have favorable effects on many indices of cardiovascular and metabolic health, including insulin sensitivity, lipid profile, indices of inflammation, endothelial function, cardiac parasympathetic activity, and carotid IMT (10;44;67-72). It appears that the favorable effects of physical activity on lipids are clearest in youth who exhibit an especially elevated risk status at baseline (10;69). Some studies have shown that physical activity interventions led to improvements in insulin sensitivity or lipid profile that were to some degree independent of changes in body fatness (73-75). However, obese youth who participated in a school-based physical activity intervention and who improved in fitness, fatness and fasting insulin concentration (76), lost their gains over the subsequent summer when they were not engaged in regular physical activity (77). This shows the importance of maintaining exposure to physical activity on a long-term and continuous basis.

In contrast to results from physical activity intervention studies in obese youth, studies of youth who varied over the spectrum of fatness at baseline, have generally failed to provide evidence that physical activity reduced fatness or improved risk profiles (7;78;79). This discrepancy between the results of observational and intervention studies suggests that the dose of physical activity needed in these subjects may be greater than that needed to elicit such changes in obese youth. Research is needed on the impact of physical activity interventions carried on for extended periods of time. Because of the difficulty of conducting RCTs over the periods of time needed to produce substantial changes in body fatness (i.e., years rather than months), conclusive evidence from RCTs is quite difficult to obtain.

An important aspect of the physical activity–health relationship is the dose of physical activity that is associated with favorable risk status. However, relatively little clear information is available on this matter. The limited information available from observational studies suggests that at least 360 minutes per week of moderate-to-vigorous physical activity is associated with a good risk profile (53). With respect to a desired intensity of physical activity, some evidence indicates that vigorous physical activity, such as that found in sports, may be more closely related to a favorable risk status than is moderate physical activity (51;58). This is consistent with studies showing that vigorous physical activity, more so than moderate physical activity, is associated with lower amounts of fatness (80-83).

In the general population of youth, few experimental data exist to show a beneficial effect of physical activity on fatness or risk status, perhaps because the few investigations available used relatively small doses of physical activity. It is likely that doses of controlled moderate-to-vigorous physical activity greater than 300 minutes per week are needed for such youth to prevent accretion of general and visceral fat (35). Even when an intervention that employed a dose of this size had a favorable effect on fatness, the changes in risk profile of the intervention and control groups did not reach significance (42). It may be necessary for youth to maintain the lower levels of fatness for years in order to see clear effects on the fatness-associated risk profile.

Taken together, the observational and experimental evidence supports the hypothesis that maintaining high amounts and intensities of physical activity starting in childhood and continuing into the adult years will enable people to maintain a favorable risk profile, less end-organ damage, and lower rates of morbidity and mortality from cardiovascular disease and type 2 diabetes mellitus. Taken collectively, the research suggests that moderate-to-vigorous physical activity for at least 1 hour per day would help youth to maintain a healthy cardiovascular disease and type 2 diabetes risk profile. Higher volumes or intensities of physical activity probably have greater benefit.

Conclusions on Developmental and Demographic Influences

Very little is known about the effects of age, developmental status, sex, race/ethnicity, and socioeconomic status on the relation of physical activity to cardiovascular disease and type 2 diabetes risk status.

Rationale for Developmental and Demographic Influences

Very few studies have investigated interactions of physical activity with age, developmental status, sex, race/ethnicity, or socioeconomic status. Of those that have investigated such interactions, some have reported contradictory findings. For example, a study of Danish children found that physical activity was inversely related to insulin resistance in girls, but not in boys (61) whereas a study of American youth found the opposite result, namely that greater physical activity was associated with better insulin sensitivity in boys, but not in girls (63). Thus, interactions of physical activity with these factors are an important topic for future investigations.

Question 5: Is Physical Activity Significantly Related to Bone Health in Children and Adolescents? If So, Is There an Established Dose-Response Pattern? Is the Relation Influenced by Age, Developmental Status, Sex, Race/Ethnicity, or Socioeconomic Status?

Conclusions on Relation and Dose-Response Pattern

Bone-loading physical activity increases bone mineral content and density. Targeted weight-loading activities that simultaneously influence muscular strength, done 3 or more days per week are effective. It is challenging to compare mode and dose, as some studies observed or implemented jumping activities, some used weight-bearing games, and some examined resistance training activities. Intensities are reported as ground-reaction force (GRF), levels from moderate to vigorous, or as a percent of the 1RM. Rarely do doses vary within a study, supporting the need for dose-response studies.

Rationale for Relation and Dose-Response Pattern

The literature from 1995 to the present yielded 17 RCTs, 5 group randomized trials (2 of which published follow up data 9 to 12 months after study completion), and 7 prospective cohort studies that examined the relation between physical activity and bone health. Specific outcome measures included at least one of the following: bone mineral content (BMC), bone mineral density (BMD), bone area (BA), stiffness index (SI), bone geometry and strength, and periosteal circumference.

The osteogenic potential of physical activity is determined by the magnitude of the external load, the dynamic nature of the load, the rate at which the load is introduced, and the duration of the loading bout (84). Weight-bearing activities that introduce stress to the skeleton through either GRF (e.g., running, jumping) or high-intensity joint-reaction forces (e.g., weight lifting) have a greater effect on bone mineral accretion than do weight-supported activities (e.g., bicycling, swimming), and may be more effective in reducing future risk of osteoporosis (85).

Studies that report a GRF show a minimum load or dose of 3X body weight (BW) to be effective in changing BMC. Short duration bouts with GRF more than 5X BW have produced effects in the femur (86) and tibia (87), compared to growth-related changes in controls participating in usual weight-bearing activity during physical education classes, with loads less than 5X BW.

Studies that focused on high-intensity jumping (at least 3X BW) for 3 to 12 minutes at a time, at least 3 days per week, showed an effect on femoral neck or greater trochanter BMD (37;88-90). Adding high-intensity weight-bearing physical activity (12 minutes, 3 times per week) to school-based physical education classes resulted in positive gains in BMC of the spine and hip after 7 months in early pubertal girls and pre-pubertal boys and then at 20 months in pre-pubertal boys and pubertal girls (36;37;88;91). Boys also demonstrated changes in bone structural geometry (bone strength) after 20 months.

In most studies, an exercise or physical activity regimen of at least 2 days per week (35) and up to 5 days per week (87;92) resulted in positive effects on bone health. Most studies implemented the intervention 3 days per week (36;37;88;90;91). The majority of studies have been conducted over a 6 to 20 month period. A duration of only 6 months was too short to demonstrate significant changes in some of the studies (93) and yet one study showed a positive effect after just 4 months of high-intensity jumping rope (GRF=3.2 X BW) in girls aged 14 to 15 years (94).

Conclusions on Developmental and Demographic Influences

The relation between physical activity and bone health is influenced by age and developmental status. A number of studies suggest that the window of opportunity for the effects of physical activity on bone mineralization in both boys and girls is during early puberty and pre-menarchal years. During the period of peak BMC velocity (12.7 years for girls; 14.1 years for boys), a greater increase in BMC is seen for highly active than less active children. The bone health of both boys and girls is improved by physical activity. Limited information is available about the influence of race/ethnicity because most studies examined only white children and many studies did not report race at all. Most of the published studies do not routinely present data on socioeconomic status, so it is difficult to determine whether differences exist on this demographic parameter.

Rationale for Developmental and Demographic Influences

Age and/or Developmental Status

The effect of mechanical loading on the skeleton is dependent on both age and maturity (i.e., hormone levels) (95), particularly around the peak BMC velocity. A number of recent studies showing positive effects from physical activity suggest that the window of opportunity for bone mineralization effects resulting from the activity, in both boys and girls, is during early puberty and pre-menarchal years (36;90;91;96-99). Recently, MacDonald and colleagues showed an effect on distal tibia strength in pre-pubertal boys, not girls, using peripheral quantitative computed tomography (pQTC), after a 16-month intervention period (87). These studies have shown effects for trabecular bone in particular, although some have demonstrated an effect on cortical bone (87;99). Some studies in menarchal or post menarchal girls have not shown greater improvements in bone mineral content compared to controls (93;100;101), though others have shown improvement (37;94;102;103). It is difficult to put an age to the prepubescent period because increases in obesity boost adiposity, which may influence the biologic age at which it occurs and hence the window of opportunity. However, most of the prepubertal studies have examined 8-12 year olds and the pubertal/post pubertal studies have examined 12-15 year olds. Only one study examined preschoolers ages 3 to 5 years (92), and found an increase in periosteal circumference after 12 months of gross motor physical activity.

Physically inactive children may fail to realize their potential for peak bone mass during the growing years, particularly the pre-pubescent and pubertal period. Given the inadequate levels of physical activity among American youth of all ages, the long-term consequences on bone health may present a serious disease burden in future decades. Therefore, from a public health perspective it is difficult to confine the advice to youth who are verging on or at puberty.

Sex

The bone health of both boys and girls benefits from physical activity. The majority of studies focused on girls, but 4 randomized studies have shown effects in boys, all of whom were pre-pubertal at baseline (87;88;91;96).

Race/Ethnicity

Most of the studies have been performed with white children and some with Asian children (36;37;88;91), although many studies do not report race/ethnicity at all. Barbeau recently reported the gains in total body BMD in black girls ages 8 to 12 years after a 10-month physical activity program (35). This study showed a positive relation between gains in fitness and increases in total body BMD and BMC.

Socioeconomic Status

Most of the published RCT and group RCT studies did not present data on socioeconomic status so it is difficult to determine whether such differences exist.

Question 6: Is Physical Activity Significantly Related to Mental Health in Children and Adolescents? If So, Is There an Established Dose-Response Pattern? Is the Relation Influenced by Age, Developmental Status, Sex, Race/Ethnicity, or Socioeconomic Status?

Conclusions on Relation and Dose-Response Pattern

Physical activity during childhood and adolescence exerts a beneficial effect on several mental health outcomes. These include symptoms of anxiety and depression, self-esteem, and physical self-concept. The varying methodologies and insufficient numbers of intervention trials preclude inferences about dose-response patterns.

Rationale for Relation and Dose-Response Pattern

Although the burden of poor mental health is understudied in youth, the prevalence of psychiatric disorders and symptomatology is known to be substantial. The lifetime prevalence of major depression among youth has been estimated to be between 15% and 20% (104). Twice as many female as male youth have reported symptoms of major depression (105). An even broader spectrum of mental well-being is particularly relevant to youth populations, including self-esteem and academic performance.

A burgeoning body of evidence documents the effects of physical activity on neurological and psychological processes in adults, and the number of studies in children and adolescents also is growing. The evidence for the former has been described in detail elsewhere in this report in ***Part G. Section 8: Mental Health***. The quality of the evidence base for youth, especially the relatively few RCTs and longitudinal population-based cohort studies, constrain the aspects of mental health that may be examined in this brief synthesis. Although a limited number of studies have examined the association between physical activity and mental health among youth, they indicate an inverse association between physical activity and depressive symptoms (15;106-114) and anxiety (15;107;110;111;114). Studies also indicate a positive association between physical activity and self-esteem and self-concept (14;107;111;115-119). In addition, some research studies indicate an association between physical activity and academic performance (42;108;120-122). Twelve primary research articles were reviewed: 1 randomized controlled trial, 2 group RCTs, 2 prospective cohort studies, 3 non-randomized trials, and 4 cross-sectional studies. The outcomes targeted in these studies were depressive symptoms, anxiety, academic performance, and self-esteem/ self-concept.

Depressive Symptoms

Of the 6 identified studies that measured depressive symptoms, 2 were intervention trials (one randomized and one non-randomized), 1 was a prospective cohort study, and 3 were cross-sectional studies.

The randomized trial was a 12-week intervention implemented in 66 Hispanic fourth graders (15). The aerobic group participated in physical activities and maintained a mean heart rate of 134 beats per minute for 20 minutes, 3 days per week (15). The authors concluded that the moderate to vigorous physical activity obtained during the intervention reduced depressive symptoms (15). Annesi and colleagues (109) implemented a 12-week non-randomized intervention among 90 children aged 9 to 12 years, and found a significant decrease in depression and a significant improvement in mood. Too few intervention trials were found to permit assessment of dose-response or separate influences of different activity types.

Motl and colleagues (106) followed 7th graders prospectively for 2 years and assessed non-school related physical activity and depressive symptoms. They determined that changes in physical activity were inversely related to changes in depressive symptoms over the 2-year period (106). Recent longitudinal cohort studies also have suggested associations between lower levels of emotional symptoms and peer problems among boys who were physically active 3 years earlier (117).

All of the 3 cross-sectional studies found an inverse relation between physical activity and depressive symptoms. Parfitt and Eston (107) measured physical activity objectively with pedometers, and depression with the Childhood Depression Inventory among 70 children aged 10 years, and they reported an inverse correlation between physical activity and depressive symptoms ($r = -0.60$) (107). The 2 other cross-sectional studies measured sports participation and depressive symptoms of 89 youth in 12th grade (108) and 1,038 high school students (110). Field and colleagues (108) reported that youth who were more physically active had significantly less depressive symptoms than their less-active peers, and Pastor and colleagues (110) reported a negative correlation between sports participation and depressive symptoms ($r = -0.14$). A recent expert panel review also found cross-sectional data that demonstrated weak inverse associations between physical activity and scores on measures of depressive symptoms (123).

Further, the same expert panel review found quasi-experimental studies that showed strong positive effects of physical activity in decreasing anxiety scores (123). Too few intervention trials were found to permit assessment of dose-response or separate influences of different activity types, however. Several recent cross-sectional studies have linked higher levels of physical activity to higher mental health scores and fewer feelings of sadness and suicidal ideation in ethnically and/or socioeconomically diverse samples, although evidence is insufficient to draw conclusions about differential sociodemographic effects (124;125).

Anxiety

Of the 3 identified studies that measured anxiety, 1 was a randomized trial, and 2 were cross-sectional studies. One of the cross-sectional studies, which focused on children aged 10 years (107), found an inverse association between objectively measured physical activity and anxiety ($r = -0.48$). In the other, which examined a large sample of high school students (n=1,038), Pastor and colleagues (110) reported a small, but significant inverse relation between sports participation and anxiety ($r = -0.07$). Conversely, a randomized trial of 66 Hispanic children in 4th grade did not produce changes in anxiety symptoms (15). The recent expert panel review mentioned previously found cross-sectional data to have demonstrated weak inverse associations between physical activity and scores on measures of anxiety symptoms (123).

Academic Performance

Four studies assessed the relation between physical activity and academic performance: 2 group RCTs, 1 prospective cohort study, and 1 cross-sectional study. Sallis and colleagues (120) administered the SPARK physical education program among 754 children in 4th to 6th grade, using 2 levels of implementation (Physical Education Specialists and Trained Teachers) compared to a control group (standard physical education). The SPARK program consisted of 30-minute sessions at least 3 times per week. Academic performance was measured with the Metropolitan Achievement Tests (120). The authors concluded that the SPARK program had a favorable effect on academic achievement. The students in the Specialist condition had significantly higher reading scores compared to the control group, and the students in the Trained Teacher condition had significantly higher language, reading, and basic battery scores compared to the control group (120). In addition, the SPARK program had no detrimental effects on academic performance even though it involved a significant investment of time (2 times the amount of instruction per week compared to the control group) (120).

Yin and colleagues (42) implemented the Georgia FitKid Project among 525 children in 3rd grade. The program consisted of 80-minute physical activity sessions 3 days per week, and academic performance was assessed with criterion-referenced competency tests. The authors reported no differences in academic scores between the intervention group (with 40%+ attendance) and the control group (42).

The 2 remaining studies found a positive relation between physical activity and academic performance. A total of 214 children in 6th grade were observed prospectively, and youth who met the Healthy People 2010 vigorous physical activity standards had higher academic scores compared to their peers who did not meet the standards (121). Field and colleagues (108) reported a cross-sectional positive association between physical activity and grade point average.

These findings are consistent with recent reviews of the literature. Although observational studies have consistently found relationships between physical fitness and grades and test scores, those between physical activity and direct measures of academic achievement often have had null findings (126;127). Similarly, intervention studies have been few in number, often had design weaknesses, and infrequently demonstrated improvements in academic achievement (126;127). They have, however, generally found no decrements in academic outcomes, despite substitution of activity time for didactic instruction (126). Salutary effects on indirect measures of academic performance, such as on-task behavior, disruptiveness, memory, concentration, and homework completion, have more consistently been linked to physical activity (123;126;128).

Self-Esteem and Self-Concept

DeBate and colleagues (115) assessed the impact of the *Girls on the Run* program on self-esteem of 322 girls aged 8 to 12 years. The program consisted of 60-minute sessions 2 days per week, and self-esteem was measured with the Rosenberg self-esteem scale (115). The authors concluded that self-esteem increased significantly (115). In a cross-sectional study of 70 children aged 10 years, physical activity (assessed by pedometry) was positively associated with global self-esteem (r = 0.66) (107). Annesi and colleagues (14) implemented a non-randomized trial among 570 African American children that consisted of physical activity sessions for 45 minutes, 3 days per week for 12 weeks. They determined that exercise self-efficacy increased among girls aged 9 to 12 years, but no changes were detected in boys or younger girls (14). Lastly, Dishman and colleagues (116) reported a positive association between physical self-concept and physical activity among 1,250 girls in 12th grade.

Conclusions on Developmental and Demographic Influences

It is difficult to draw conclusions about age and sex because most relevant studies have included children or adolescents within a narrow range of ages and a single sex, precluding sub-group analyses by age or sex. Favorable influences have been reported across age groups, but within-study comparisons have not generally been reported. Similarly, most studies do not analyze data by race/ethnicity or socioeconomic status; therefore, it is difficult to make conclusions about their influence on the relation between physical activity and mental health.

Overall Summary and Conclusions

The subcommittee’s review of the scientific literature supports the overall conclusion that physical activity provides important health benefits for children and adolescents. This conclusion is based on findings of observational studies in which higher levels of physical activity were found to be associated with more favorable health parameters as well as experimental studies in which exercise treatments caused improvements in health-related factors. The documented health benefits include increased physical fitness (both cardiorespiratory fitness and muscular strength), reduced body fatness, favorable cardiovascular and metabolic disease risk profiles, enhanced bone health, and reduced symptoms of depression and anxiety.

The types and amounts of physical activity required to produce health benefits vary across the health outcomes. Also, because of limitations in the scientific evidence base, it is not possible to draw definitive conclusions regarding the minimal or optimal doses of physical activity needed to provide health benefits in young persons. Nonetheless, considering all the evidence, the subcommittee concluded that important health benefits can be expected to accrue to most children and youth who participate daily in 60 or more minutes of moderate to vigorous physical activity. Further, the subcommittee concluded that certain specific types of physical activity must be included in an overall physical activity pattern in order for children and youth to gain comprehensive health benefits. These include regular participation in each of the following types of physical activity on 3 or more days per week: resistance exercise to enhance muscular strength in the large muscle groups of the trunk and limbs, vigorous aerobic exercise to improve cardiorespiratory fitness and cardiovascular and metabolic disease risk factors, and weight-loading activities to promote bone health. It is the subcommittee's judgment that these specific types of physical activity can be appropriately performed to create a 60 minute or more per day activity pattern.

The subcommittee was not charged with considering the scientific literature on behavioral and programmatic interventions to provide and promote physical activity in children and youth. Nonetheless, the subcommittee feels strongly that young persons should obtain their health-promoting physical activity in ways that will allow them to attain health benefits over the short term as well as encourage them to maintain a physically active lifestyle over the long term. Experiences that are consistent with these goals involve participation in physical activities that are developmentally appropriate, that minimize the potential risks of overtraining and injuries, and that provide participants with opportunities for enjoyable participation in a wide range of specific forms of physical activity.

Research Needs

In reviewing the scientific literature, it became apparent that many research needs exist regarding the health benefits of physical activity among youth. Specifically, the subcommittee recommends that research be conducted to:

- Determine the types and amounts of physical activity that are needed to prevent the development of excessive adiposity during childhood and adolescence;
- Establish the dose-response pattern for the relation between physical activity and bone health in children and adolescents;
- Identify the optimal types and amounts of physical activity to maintain cardiovascular and metabolic health during childhood and adolescence;
- Determine whether physical activity affects classroom behavior and academic achievement in children and adolescents; and
- Determine the extent to which age, developmental status, sex, race/ethnicity, and socioeconomic status influence the effects of physical activity on body composition, cardiovascular and metabolic health, bone health, and mental health.

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Part G. Section 10: Adverse Events

Introduction

The benefits of regular physical activity outweigh the inherent risk of adverse events. Still, adverse events are common even if usually not severe and are an impediment to widespread participation in regular physical activity (1-4). Awareness of the types and causes of activity-associated adverse events can be helpful. Selection of low risk activities and prudent behavior while doing any activity can minimize the frequency and severity of adverse events and maximize the benefits of regular physical activity.

Physical activity-related adverse events are undesired health events that occur because a person is physically active. They may be mild or severe and include such diverse maladies as musculoskeletal injuries, cardiac arrhythmias, heat injuries, and infectious diseases. Musculoskeletal injuries are the most common type of physical-activity associated adverse event, have generated the most scientific study, and are the primary focus of this chapter. Musculoskeletal injuries may be sudden, such as a torn anterior cruciate ligament in the knee in a soccer player, or slow to develop, such as pain around the knee due to the iliotibial band syndrome in a runner or hiker. The current scientific literature does not routinely distinguish between these two types of injuries, sometimes referred to as traumatic and overuse, despite the value of doing so.

The chapter also considers in detail sudden adverse cardiac events because they may result in severe outcomes (e.g., death, myocardial infarction), fear of them likely reduces participation in activity, and their occurrence can be reduced. Other types of adverse events (e.g., heat-related illness, infections) are mentioned largely to provide examples and maintain awareness of the broad array of potential adverse events.

The factors that increase susceptibility to these adverse events also are diverse, and include the type of activity being performed (e.g., walking versus rugby), the dose of activity (the amount, as determined by the frequency, duration, and intensity), personal characteristics (e.g., age, physical activity habits), equipment or protective gear used (e.g., bike helmets), and environmental conditions (e.g., proximity to traffic, weather) (Table G10.1).

Table G10.1. Factors Associated With the Risk of Activity-Associated Adverse Events

1. Type of activity*
2. Dose of activity*
3. Personal characteristics
a. Demographic
b. Behavioral*
c. Health status
4. Protective gear and equipment
5. Environmental conditions

*Key factors under individual control

Whenever possible, the chapter draws from studies of the general population rather than research on elite or competitive athletes. Much of the research in this area has focused on competitive athletes. The frequency, duration, and intensity of the exposure and, sometimes, even the rules of the game differ markedly between competitive athletes and the general population, making extrapolation from the injury experiences of competitive athletes to the general population likely to be misleading.

While considering both the spectrum of adverse events and their causes, the chapter emphasizes the key factors of any physical activity program:

- The type (mode) of activity;
- The dose of activity as determined by the frequency, duration, and intensity of participation; and
- The rate of progression or change in the amount of activity (5).

These 3 factors are largely under individual control, and though the exact proportion of adverse events attributable to decisions in just these areas is not known, it is likely substantial. The risk of injury varies widely for different types of activities, with low-impact activities, such as walking or gardening, associated with the fewest musculoskeletal injuries. A higher dose of activity, especially among those who have previously not been active, is associated with more musculoskeletal injuries. Finally, modest and gradual increments in frequency and duration of activity are preferred at the beginning of any effort to increase aerobic activity. Augmentation of intensity, if desired, should come later (6). Attaining the desired level of activity may require a year, especially for elderly, obese, or habitually sedentary individuals (7).

Although the risk of activity-related injury is greater among persons who are more active, the risk of other types of injuries (e.g., motor vehicle, work-related) may be less, making the overall risk of injury for active people no greater than that for sedentary people. Only two population-based studies have examined this issue. One reported that people who ran or participated in sports activities were about 50% more likely to report an injury (activity-related or not) than people who reported walking for exercise or were sedentary (8). The other reported no significant differences in overall injury rates (activity-related or not) between inactive people, irregularly active people, and people who met current recommendations for physical activity (9). More studies of this type are needed, but it is possible that regular physical activity may cause some injuries and prevent others, and that physically active people may have no more injuries than sedentary individuals.

Review of the Science

Overview of the Questions Asked

The 5 major questions addressed in this chapter are:

1. What types of activities have the lowest risk of musculoskeletal injuries?
2. How does the dose of physical activity affect the risk of musculoskeletal injury?
3. Are individuals at increased risk of sudden adverse cardiac events when they are being physically active?
4. What general factors influence the risks of musculoskeletal injury and other adverse events related to physical activity?
5. Do the benefits of regular physical activity outweigh the risks?

Data Sources and Process Used To Answer Questions

The Adverse Events subcommittee used the *Physical Activity Guidelines for Americans* Scientific Database developed for the PAGAC process for this chapter (see ***Part F: Scientific Literature Search Methodology***, for a detailed description of the Database). The diversity of exposures, mediators, and outcomes plus the limited number of recently published papers on several important topics required an expanded search for pertinent work. The subcommittee therefore conducted special literature searches on upper respiratory infections and medical expenditures and added these publications to the Scientific Database. A literature search pertaining to air pollution and health was conducted but not added to the Database because physical activity was not a required component of the search. Additional citations were drawn from the Institute of Medicine's summary report of the Workshop on Adequacy of Evidence for Physical Activity Guidelines Development (10), review articles, consultants' recommendations, and other citations in pertinent articles.

Question 1. What Types of Activities Have the Lowest Risk of Musculoskeletal Injuries?

Conclusions

Activities with fewer and less forceful contact with other people or objects have appreciably lower injury rates than do collision or contact sports. Walking for exercise, gardening or yard work, bicycling or exercise cycling, dancing, swimming, and golf, already popular in the United States, are activities with the lowest injury rates.

Rationale

Risk of musculoskeletal injury varies substantially across different activities and is determined to a large extent by the frequency and force of collisions or contact with other people, the ground, or other inanimate objects. Categorization of activities by risk is difficult because style and rules of play vary by age, location, and other factors. However, the Committee on Sports Medicine and Fitness has proposed general categories that provide a guide to the injurious forces associated with specific activities (11). In collision sports (e.g., football, ice hockey, wrestling) participants purposefully hit or collide with each other or inanimate objects. In contact sports (e.g., basketball, soccer) participants make contact with each other but usually with less force. In limited-contact sports (e.g., baseball, ultimate Frisbee) participants' contact with other players or objects is infrequent or unintentional. In non-contact sports (e.g., running, swimming, tennis) contact between participants is uncommon. In general, the risk of injury is higher for collision or contact sports than for limited- or non-contact activities.

What Types of Activities Are Associated With the Lowest Risk of Injury in the General Population?

Most of the published information about the number of injuries incurred during different types of activities does not take into account either the number of people participating in various activities or the length of time they spend doing so. As a result, tabulations of injuries seen in emergency departments or other health care settings usefully describe the load on medical care services but do not allow risk estimates for different activities at the individual level. Very few studies have provided injury rates based upon the amount of time spent doing the activities.

A survey of injury risk in the general population in Finland reported a wide range of injury risk for different types of physical activities (Table G10.2[1]) (12).

Table G10.2. Injuries per 1,000 Hours of Participation and Per 1,000 Participants by Activity, Finland (12)

Commuting Activities

Activity*	Injuries per 1,000 Hours of Participation	Estimated† Injuries per 10^6 MET-Min of Participation Value (METs)	Injuries per 1,000 Persons Reporting the Activity
Walking	0.2	0.8 (4)	23.2
Cycling	0.5	1.4 (6)	21.2

Lifestyle Activities

Activity*	Injuries per 1,000 Hours of Participation	Estimated† Injuries per 10^6 MET-Min of Participation Value (METs)	Injuries per 1,000 Persons Reporting the Activity
Hunting, fishing, berry picking	0.3	1.3 (4)	20.6
Home repair	0.5	2.1 (4)	78.2
Gardening	1.0	4.2 (4)	92.0

*Not all activities in category are shown
†MET values estimated from reference 13
‡Categories from reference 11

[1] The amount of physical activity has been measured and reported in various formats, including minutes of exposure as in this study, miles or kilometers of running per week, or kilocalories of energy expenditure. MET-minutes are being used with increasing frequency. In this chapter, whenever feasible, an estimate of exposure expressed in MET-minutes is provided. The estimate is less precise than the original measures reported in this study but may be helpful when comparing the findings from different studies. For this study, the categories used by Parkkari and colleagues (12) did not correspond exactly with the categories in the Compendium of Physical Activities (13), and approximations were made.

Table G10.2. Injuries per 1,000 Hours of Participation and Per 1,000 Participants by Activity, Finland (12) (continued)

Sports, Noncontact‡

Activity*	Injuries per 1,000 Hours of Participation	Estimated† Injuries per 10^6 MET-Min of Participation Value (METs)	Injuries per 1,000 Persons Reporting the Activity
Golf	0.3	1.1 (4.5)	35.1
Dancing	0.7	2.3 (5)	23.5
Swimming	1.0	2.4 (7)	23.6
Walking	1.2	5.0 (4)	89.7
Rowing	1.5	3.6 (7)	51.9
Pole walking	1.7	5.7 (5)	54.9
Cross-country skiing	1.7	3.5 (8)	67.2
Running	3.6	6.0 (10)	123.2
Track and field sports	3.8	7.9 (8)	318.2
Tennis	4.7	13.1 (6)	188.2

Sports, Limited Contact‡

Activity*	Injuries per 1,000 Hours of Participation	Estimated† Injuries per 10^6 MET-Min of Participation Value (METs)	Injuries per 1,000 Persons Reporting the Activity
Cycling	2.0	4.2 (8)	62.4
Aerobics, gymnastics	3.1	7.9 (6.5)	120.6
Horse riding	3.7	15.4 (4)	546.9
Downhill skiing	4.1	11.4 (6)	192.5
In-line skating	5.0	6.7 (12.5)	190.8
Volleyball	7.0	29.2 (4)	447.2
Squash	18.3	25.4 (12)	629.6

*Not all activities in category are shown
†MET values estimated from reference 13
‡Categories from reference 11

Table G10.2. Injuries per 1,000 Hours of Participation and Per 1,000 Participants by Activity, Finland (12) (continued)

Sports, Collision and Contact‡

Activity*	Injuries per 1,000 Hours of Participation	Estimated† Injuries per 10^6 MET-Min of Participation Value (METs)	Injuries per 1,000 Persons Reporting the Activity
Karate	6.7	11.2 (10)	611.1
Ice hockey	7.5	15.6 (8)	670.7
Soccer	7.8	18.6 (7)	445.0
Basketball	9.1	25.3 (6)	508.5
Wrestling	9.1	25.3 (6)	625.0
Judo	16.3	27.2 (10)	1363.6

*Not all activities in category are shown
†MET values estimated from reference 13
‡Categories from reference 11

Reported activity-related injuries per 1,000 hours of participation ranged from 0.2 for walking as a commuting activity to 18.3 for squash. Injury rates were lower for commuting activities (range 0.2 to 0.5 per 1,000 hours of participation), lifestyle activities (range 0.33 to 1.01), and noncontact sports (range 0.3 to 4.7, median 1.6) than were the rates for limited contact sports (range 2.0 to 18.3, median 4.1) and collision and contact sports (range 6.7 to 9.1, median 7.8). The findings are based on a year long population-based random survey of Finns aged 15 to 74 years, 92% of whom agreed to record all physical activity sessions of 15 or more minutes and register all acute and overuse injuries that “caused a significant complaint to the subject” and that were related to the activities. Participation rates and related injuries were reported by telephone once every 4 months. It is interesting to note that injury rates for walking and cycling during commuting activities (0.2, 0.5, respectively) were one-sixth and one-fourth the rates for walking and cycling performed as sports or recreation (1.2, 2.0, respectively). This, too, indicates that the same activity done for different purposes and with different frequency, duration, and intensity leads to different injury rates.

Four other surveys of the general population also report appreciably lower injury rates among participants of non-contact activities such as walking, bicycling, gardening, golf, or swimming (14-17). The surveys, conducted in the United States, Canada, and Australia (2 surveys), report injury rates that are not directly comparable because of differing definitions of injury (e.g., medically attended versus any injury), differing time periods (e.g., 2 weeks versus 1 year), and the inclusion of different activities. Regardless, the relative safety of non-contact activities when compared to limited-contact, contact, and collision activities is present in all reports. In the 3 surveys in which activity-specific participation rates were provided, walking was the most commonly reported activity, generally by a substantial amount (14;16;17).

What Types of Sports Have the Lowest Rates of Injury for Children, Youth, and Young Adults?

Surveys of injuries among college sports (18;19), high school sports (20), and community organized sports leagues (21) have been conducted (Table G10.3).

Table G10.3. Game and Practice Injury Rates* for Collegiate Sports (Nationwide, 1988-2004),(18;19) High School Sports (Nationwide, 1995-1997), (20) and Children's Community Organized Sports (Pittsburgh, 1999-2000) (21)

Collegiate Sports

Sport	Level of Contact†	Game Injury Rate	Practice Injury Rate
Men's baseball	Limited	5.8	1.9
Men's basketball	Collision/contact	9.9	4.3
Men's lacrosse	Collision/contact	12.6	3.2
Men's ice hockey	Collision/contact	16.3	2.0
Men's soccer	Collision/contact	18.8	4.3
Men's wrestling	Collision/contact	26.4	5.7
Men's fall football	Collision/contact	35.9	3.8
Women's softball	Limited	4.3	2.7
Women's volleyball	Limited	4.6	4.1
Women's lacrosse	Collision/contact	7.2	3.3
Women's basketball	Collision/contact	7.7	4.0
Women's field hockey	Collision/contact	7.9	3.7
Women's ice hockey	Collision/contact	12.6	2.5
Women's gymnastics	Limited	15.2	6.1
Women's soccer	Collision/contact	16.4	5.2

*Injury rate, injuries per 1,000 athlete exposures
†Categories from reference 11

Table G10.3. Game and Practice Injury Rates* for Collegiate Sports (Nationwide, 1988-2004),(18;19) High School Sports (Nationwide, 1995-1997), (20) and Children's Community Organized Sports (Pittsburgh, 1999-2000) (21) (continued)

High School Sports

Sport	Level of Contact†	Game Injury Rate	Practice Injury Rate
Boys' baseball	Limited	5.6	1.8
Boys' basketball	Collision/contact	7.1	3.4
Boys' wrestling	Collision/contact	8.2	4.8
Boys' soccer	Collision/contact	10.2	2.5
Boys' football	Collision/contact	26.4	5.3
Girls' volleyball	Limited	1.2	2.8
Girls' softball	Limited	5.9	2.7
Girls' field hockey	Collision/contact	4.9	3.2
Girls' basketball	Collision/contact	7.9	3.2
Girls' soccer	Collision/contact	11.4	3.1

Community Organized Sports (Ages 7-13 Years)

Sport	Level of Contact†	Game Injury Rate	Practice Injury Rate
Boys' baseball	Limited	24	6
Boys' soccer	Collision/contact	26	10
Boys' football	Collision/contact	43	7
Girls' softball	Limited	11	7
Girls' soccer	Collision/contact	41	9

*Injury rate, injuries per 1,000 athlete exposures
† Categories from reference 11

The methods within each survey enable comparison of injury rates among different sports within the age-group of interest (i.e., collegiate athletes, high school athletes, or children aged 7 to 13 years in organized community sports leagues) and similar enough to allow an examination of general patterns. In all surveys, an athlete participating in a practice or game was an "athlete-exposure." From 1988-1989 through 2003-2004 the National Collegiate Athletic Association used standard methods to monitor the incidence of injury in 15 men's and women's collegiate sports (18;19). Each year approximately 250 schools voluntarily participated in the surveillance system. Injuries were counted if they occurred as a result of participation in practice or game, required medical attention by a team athletic trainer, and resulted in restricted participation for one or more days. From 1995 through 1997 data were collected from 250 athletic trainers working directly with high school sports programs on a daily basis (20). Injuries were counted if they caused cessation or participation on the day of or day after the onset; in addition, all fractures or dental injuries were counted. From 1999 to 2000, injury reports were collected from coaches in the community leagues for children aged 7 to 13 years in Pittsburgh (21). Injuries were counted if a coach came onto the field to check the condition of a player, if a player was removed from participation, or if a player needed any type of first aid during an event.

In the surveys of college and high school athletes, injuries were less common in limited contact sports than collision or contact sports. Among children's community leagues, injury rates were higher for football than for baseball, softball, or soccer, but the differences between sports were less apparent than for the older youths. None of the surveys included non-contact sports such as swimming or golf. In all 3 surveys, injuries were less common in practice than games.

Question 2. How Does the Dose of Physical Activity Affect the Risk of Musculoskeletal Injury?

Conclusions

The risk of activity-related injury (but not necessarily overall injury) is directly related to a person's usual amount of physical activity. Research with a variety of populations and methods also shows that when individuals increase their usual amount of physical activity the risk of injury is related to the size of the increase. A series of small increments in physical activity each followed by a period of adaptation is associated with lower rates of musculoskeletal injuries than is an abrupt increase to the same final level.

Fewer studies are available to examine the independent contributions to injuries of the components of physical activity — frequency, duration, intensity. However, available research indicates that each component is a contributory factor and that the composite amount is a more important determinant of risk than any component by itself.

Currently available information suggests that the commonly recommended level of regular physical activity, about 500 metabolic equivalent (MET)-minutes per week, has a low (but not precisely measured) rate of associated musculoskeletal injury. However, little information has been reported about the risks of injury at this level.

Rationale

The dose of activity is determined by its frequency, duration, and intensity. Both dose and change in dose are important determinants of musculoskeletal injuries and, to a large extent, are under personal control. This is especially important because many Americans are inactive and should be encouraged to increase the amount of physical activity in which they engage. For discussion purposes, studies providing insight into the relationship between changes in dose of activity and risk of injury can be grouped into 3 categories:

- People who have self-selected their current activity program;
- People with previously differing levels of activity who all adopt the same activity program simultaneously (e.g., military recruits); and
- People with previously similar levels of activity who are assigned different but higher levels of activity (e.g., intervention research).

Evidence from each of these 3 groups of studies indicates that: 1) the amount of activity is directly related to the risk of musculoskeletal injury and 2) the change in amount of activity is directly related to risk of musculoskeletal injury. Military recruits who are the least fit or least physically active before basic training and experimental subjects who are assigned higher amounts of activity are the most likely to become injured. Stated another way, the same amount of new activity is more likely to cause injury in sedentary individuals than in active individuals. These findings suggest that a series of small increments in physical activity each followed by a period of adaptation is associated with lower rates of musculoskeletal injuries than is an abrupt increase to the same final level. Previous physical activity recommendations for children (22), adults (23), and older adults (24) have suggested gradual augmentation of activity levels to prevent injuries and improve adherence.

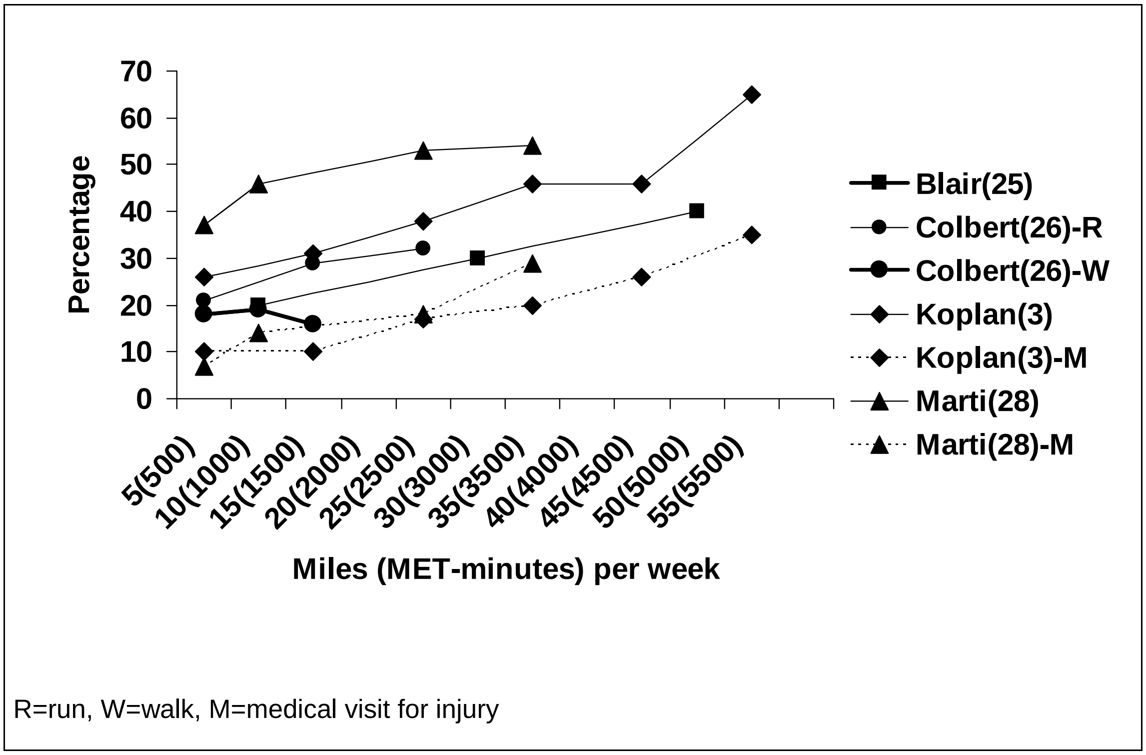
What Is the Relationship Between Self-Selected Doses of Activity and Risk of Injury?

The clearest evidence of the direct relationship between dose of activity and risk of injury comes from 7 studies of running injuries. Individuals who run 40 miles per week or more (4,000 or more MET-minutes per week)[2] are 2 to 3 times more likely to have had a running injury in the past 12 months than are individuals who run 5 to 10 miles per week (500-1,000 MET-minutes per week) (3;8;25-29) (Figure G10.1).

Five studies were retrospective cohort studies and 2 were prospective cohort studies. Injuries in all studies were self-reported but definitions varied. Three counted symptoms that caused the runner to modify his or her usual program, take medication, or seek medical advice (3;27;29), 2 counted symptoms recognized by the participant as an injury (8;28), 1 counted only injuries for which medical care was sought (26), and 1 counted only injuries that caused the runner to stop running for at least 7 days (25). Despite varying definitions, all studies reported increases in the risk of injury as the number of miles per week increased. For those studies providing information separately about injuries for which medical attention was sought, the findings were similar (3;26;28). The trends were similar for males and

[2] The speed of running is assumed to be 10 minutes per mile, an intensity of 10 METs.

Figure G10.1. Percentage of Recreational Runners or Walkers Injured by Average Number of Miles Run per Week



M, medical visit for injury; R, run; W, walk

Figure G10.1. Data Points

Study	5 (500)	10 (1000)	15 (1500)	20 (2000)	25 (2500)	30 (3000)	35 (3500)	40 (4000)	45 (4500)	50 (5000)	55 (5500)
Blair (25)	–	20	–	–	–	30	–	–	–	40	–
Colbert (26)-R	21	–	29	–	32	–	–	–	–	–	–
Colbert (26)-W	18	19	16	–	–	–	–	–	–	–	–
Koplan (3)	26	–	31	–	38	–	46	–	46	–	65
Koplan (3)-M	10	–	10	–	17	–	20	–	26	–	35
Marti (28)	37	46	–	–	53	–	54	–	–	–	–
Marti (28)-M	7	14	–	–	18	–	29	–	–	–	–

females and for runners of different ages. No information about race or ethnicity is reported by any of these studies. Similar findings have been reported for triathletes, another group for which estimating the dose of activity is relatively straightforward (30;31).

What Are the Relative Importances of Frequency, Duration, and Intensity to the Risk of Musculoskeletal Injury?

Although the evidence is limited, in these studies of runners the total dose of running appears to be more important than any of its components. Among the studies of running injuries, only 2 reported information about the relationship between frequency and injury risk. One reported that greater frequency (number of days per week of running) was significantly related to injury even after total dose (i.e., miles per week) and other factors were taken into account (29); the other reported that the relationship was not significant after adjustment for other factors, including total amount (27). Two studies reported on the relationship between duration of episodes and injury. One reported a significant relationship between minutes of running per week and injury even after other factors were taken into account (8); the other, in a multivariate analysis, reported an association between the distance of the longest run per week and injury (29). None of the 4 studies that examined the usual speed of running observed a relationship after total amount and other factors were taken into account (3;25;28;29). Two of these studies, however, reported that competitive runners were more likely to be injured than recreational or noncompetitive runners (28;29). Similar findings have been reported for competitive versus club athletes in other sports (31;32). Competitiveness may be a surrogate for relative intensity, suggesting that the athletes at greatest risk of injury are those performing near the top of their capacity.

Is the Risk of Injury per Mile Equivalent for Runners With Different Weekly Mileages?

Although the risk of injury is directly related to the volume of activity, the risk per unit of exposure appears to diminish as the volume of exposure increases. Among runners, the risk of injury per mile is about 10-fold higher at 5 miles per week (500 MET-minutes per week) than 40 miles per week (4,000 MET-minutes per week) (28;33). A similar observation has been made for subjects in the Aerobics Center Longitudinal Study (34). The annual risk of injury for persons expending about 2,000 kilocalories per week (1,632 MET-minutes per week)[3] in exercise was 22% or about 11% per 1,000 kilocalories per kilogram (816 MET-minutes per week) of exercise; the annual risk for persons expending 10,000 kilocalories per week (8,160 MET-minutes per week) was 65% or about 6.5% per 1,000 kilocalories (816 MET-minutes). These findings are consistent with the suggestion that any given increase in volume of activity (e.g., adding 500 MET-minutes per week of activity) produces a greater increase in risk of injury for those who are less active than it does for those who are more active.

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[3] Assumes 1 MET-minute = 0.82 kilocalorie. Assumes 70 kilogram body weight in formula: MET-min*3.5*70/200 = kilocalorie.

What Is the Relation Between an Assigned Dose of Physical Activity and Injury Among Persons of Different Levels of Fitness or Physical Activity Habits?

Military recruits are young healthy adults who undergo 2 to 3 months of rigorous, often vigorous, aerobic and muscular training, primarily running, marching, drill, and general conditioning exercises. Typically, recruits have 5 to 6 days of activity per week with, on average, 40 minutes of running or marching, 10 minutes of drill (learning to march in unison), 10 minutes of general condition (calisthenics), and 10 minutes of stretching per day, for a weekly total of about 2,725 to 3,270 MET-minutes (35). This level of physical activity is approximately 6 times the currently recommended amount for the population (36). Recruits experience high levels of overuse musculoskeletal injuries during this period (11% to 37% for men, 22% to 67% for women) (37). The symptomatic onset of injuries corresponds closely to the dose of activity (38) (Figure G10.2).

What Factors Are Most Consistently Associated With High Rates of Musculoskeletal Injuries During Basic Training?

Low levels of aerobic fitness and prior physical activity are 2 of the most consistently observed risk factors for injuries among the recruits. Six studies have demonstrated an inverse relationship between measures of aerobic fitness and risk of injury (35;39-43) (Figure G10.3). Aerobic fitness was determined by timed distance runs ranging from 0.75 to 2.0 miles or, in one case, peak VO_2 (40). Outcomes included time loss injuries (39;40), lower extremity injuries (35), and stress fractures (41-43). Participants in the studies were either all male, all female, or stratified by sex.

These same studies have reported similar findings for a variety of measures of pre-training physical activity practices, including frequency of running, frequency of physical activity producing a sweat, frequency of physical activity in general, self-assessed physical activity levels, and self-assessed relative fitness level (35;39-43). Similar findings have been reported when the recruits have been followed beyond the initial basic training period (44;45). Students in physical education classes (46) and participants in aerobic dance classes (47) also have been shown to be more likely to be injured if they are less physically active outside of class.

Modifications of the basic training program (e.g., less running) (48;49) or providing a formal pre-training program to recruits with low fitness (50) have resulted in reductions in the incidence of injuries among recruits in basic training while maintaining fitness goals (51).

Figure G10.2. Hours of Drill per Marching Plus General Conditioning (Solid Line, Left Axis) and Injuries per 100 Recruits (Dotted Line, Right Axis) by Week of Training

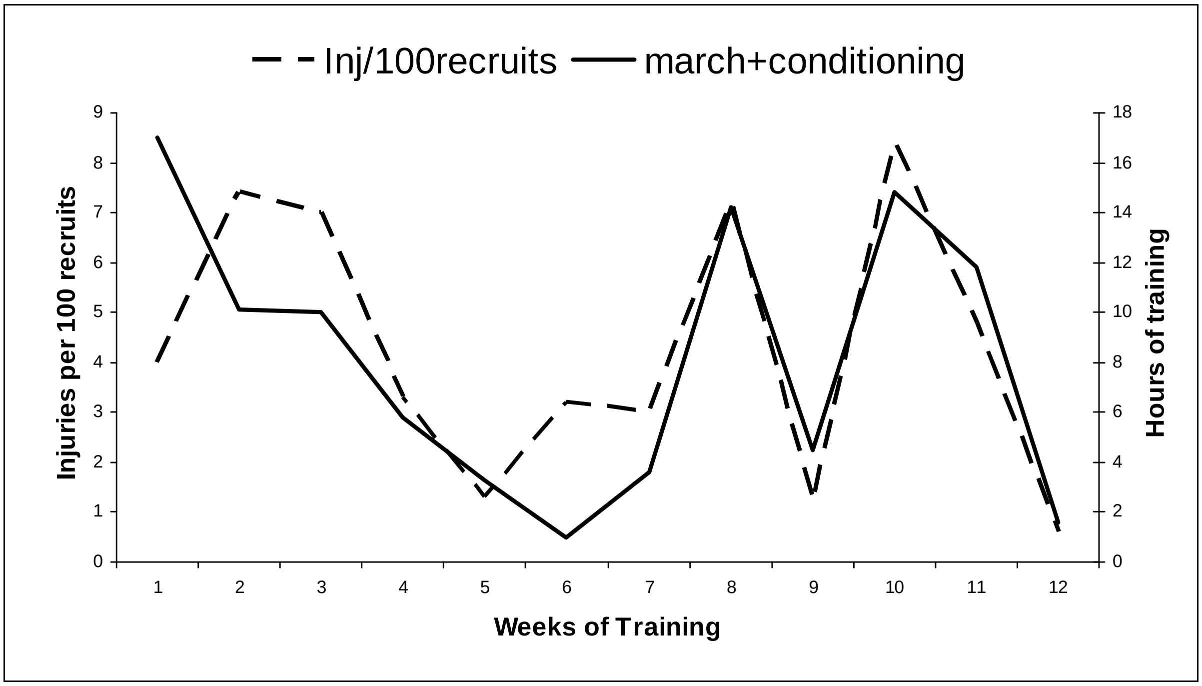
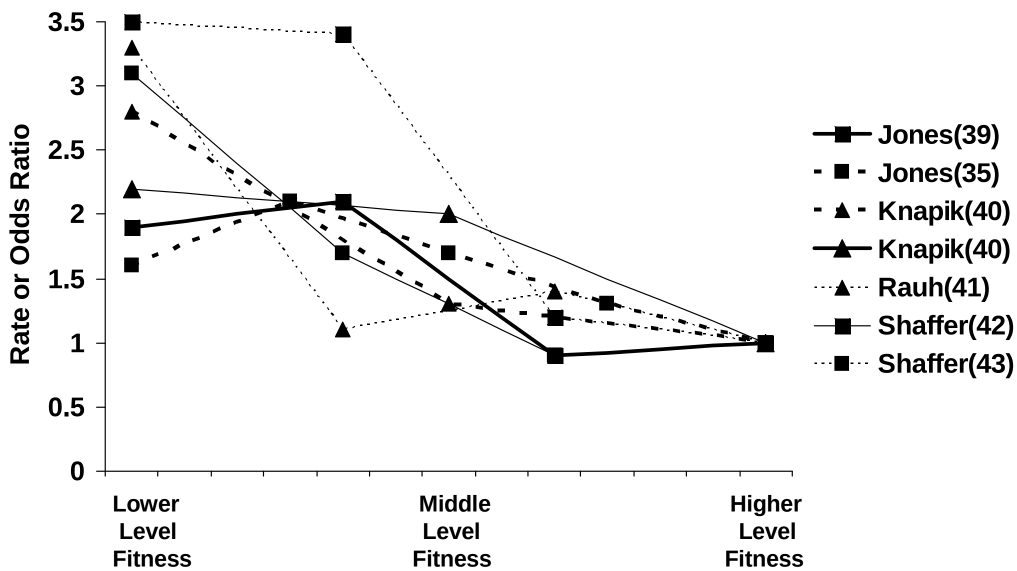


Figure G10.2. Data Points

Weeks of Training	Injuries per 100 recruits	March+conditioning
1	4.0	17.0
2	7.4	10.1
3	7.0	10.0
4	3.3	5.8
5	1.3	3.3
6	3.2	1.0
7	3.0	3.6
8	7.2	14.2
9	1.2	4.5
10	8.4	14.8
11	4.8	11.8
12	0.6	1.6

Figure G10.3. Rate or Odds Ratio for Injury Among Military Recruits During Basic Training by Aerobic Fitness at Entry



Solid lines=males, dotted lines=females, boxes=bivariate, triangles=multivariate
Rauh(41), Shaffer(42), Shaffer(43) limited to stress fracture injuries

Figure G10.3. Data Points

Study	Fitness Level 0	Fitness Level 1	Fitness Level 2	Fitness Level 3	Fitness Level 4	Fitness Level 5	Fitness Level 6	Fitness Level 7	Fitness Level 8	Fitness Level 9	Fitness Level 10	Fitness Level 11	Fitness Level 12
Jones (39)	1.9	–	–	–	2.1	–	–	–	0.9	–	–	–	1
Jones (35)	1.6	–	–	2.1	–	–	1.7	–	–	1.3	–	–	1
Knapik (40)	2.8	–	–	–	–	–	1.3	–	–	–	–	–	1
Knapik (40)	2.2	–	–	–	–	–	2	–	–	–	–	–	1
Rauh (41)	3.3	–	–	–	1.1	–	–	–	1.4	–	–	–	1
Shaffer (42)	3.5	–	–	–	3.4	–	–	–	1.2	–	–	–	1
Shaffer (43)	3.1	–	–	–	1.7	–	–	–	0.9	–	–	–	1

Are These Findings Consistent With Principles of Exercise Training Programs?

The findings in military recruits, students, and runners are consistent with the 2 major principles of exercise training programs: 1) overload and adaptation, and 2) specificity of response (52). The overload and adaptation principle states that function is improved when tissues (e.g., muscles) and organs (e.g., heart) are exposed to an overload (i.e., a stimulus greater than usual) and provided time to recover and adapt. Repeated exposures to a tolerable overload are followed by adaptation of the tissues and organs to the new load and improvements in performance and function. Too large an overload or insufficient time for adaptation, however, leads to injury and malfunction. The principle of specificity states that the adaptation and improved function is limited to the tissues and organs that have been overloaded. Training the muscles of the legs, for example, does not improve strength in the arms and shoulders.

In summary, these studies indicate that the risk of musculoskeletal injury is directly proportional to the gap between one's accustomed level of activity and the level of activity currently being performed. The larger the overload the smaller the chance of adaptation and the greater the chance of injury.

What Is the Relation Between Different Assigned Doses of Physical Activity and Injury Among Persons of Similar Levels of Fitness or Physical Activity Habits?

Assigning different physical activity regimens to groups of people who are otherwise similar would provide experimental evidence about the relative risks of different activity regimens. Although substantial numbers of clinical trials with physical activity as an exposure have been done in recent years, information about musculoskeletal injuries incurred during the trials and their relation to dose of activity is sparse. Comparison among studies is difficult because the assigned activity, outcome measures, period of study, and level of detail about injuries differ markedly (Table G10.A1, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/).

The amount and type of information has varied over time. Earlier reports that included males aged 25 to 60 years, and used vigorous activity reported high injury rates, nearly 50% (53-55). A few studies specifically investigated the relationship between the dose of activity and the incidence of injury (56-59) and, taken together, have reported that the incidence of injury appears to be related to each of the components of dose, frequency, duration, and intensity. More recent research has focused on interventions to promote moderate intensity physical activity. These studies suggest that the incidence of injuries attributable to recommended levels of moderate intensity physical activity appear to be low (60-65), but their actual incidence, severity, and effect on long-term physical activity participation are largely unknown. The study for which injury rates for both intervention and control subjects appeared to be most thoroughly reported found equivalent rates of musculoskeletal problems (64). A systematic review of interventions to prevent lower limb soft tissue running injuries concluded "it is not possible to suggest an optimal training load" (66), but that injuries are associated with frequency, duration, intensity, or total amount of training.

An observation noted in both early and more recent publications is the apparent frequency of injuries during the first weeks of the intervention (53;67). One researcher advocated 8 to 10 weeks of preparative training before actually beginning a trial (53); another reported that half of all injuries occurred within the first 4 weeks of a 24-week program (67).

In summary, reports from experimental studies suggest that frequency, duration, and intensity all contribute to the risk of physical activity-related adverse musculoskeletal events, that a substantial increase in activity level leads to high rates of musculoskeletal problems, and that moderate intensity physical activity appears to have low (but not precisely measured) injury rates.

Are Injury Rates for Walking Less Than Injury Rates for Running?

On the surface, musculoskeletal injury rates from walking appear to be less than injury rates for running. Annual injury rates among runners range from 12% to 50% (median 35%) (2;3;12;25;27-29); for walkers they range from 3% to 20% (2;12;16;17). A direct comparison of injury rates for joggers and walkers reported rates of 75% and 54%, respectively, for all reported injuries, and 25% and 21%, respectively, for injuries requiring 7 days of inactivity (59). In a study of injury and adherence rates, the injury rate increased from 5% during the 13 weeks of mostly walking to 57% during the weeks of mostly jogging (56).

The apparent differences in injury rates for walking and running deserve closer scrutiny, however. Although the higher injury rates for running compared with walking are generally assumed to be due to higher impact forces (68) and greater tension on muscles and tendons, some or all of the difference may be due to the higher volume of activity performed by runners. For example, the relative difference in injury risk between people walking or running for recreation or sport is larger when the exposure is minutes of participation (1.2 versus 3.6 injuries per 1,000 hours of participation) than when the exposure is MET-minutes of participation (5.0 versus 6.0 injuries per 10^6 MET-minutes of participation) (Table G10.2) (12). In addition, 19% of persons expending 600 MET-minutes per week while walking were injured compared with 21% of persons expending 700 MET-minutes per week while running (Table G10.A2, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/) (26). Data such as these suggest the risk of injury from walking or running depends largely upon the total amount of energy expended. At least 2 studies, however, have reported that the risk of injury attributable to walking is seemingly independent of volume for reasonable volumes (8;26;69). In one case, the volume of walking was largely determined by walking more minutes per session (8;26), in the other by using inclined treadmills to raise the intensity (69).

To summarize, it is not yet certain whether walking is intrinsically safer than running or whether the reported lower rates of injury from walking are because the total volume of activity (combination of duration, frequency, and intensity) is less for walkers than for runners.

Question 3. Are Individuals at Increased Risk of Sudden Adverse Cardiac Events When They Are Being Physically Active?

Conclusions

During periods of vigorous physical activity all individuals, even regularly active individuals, are at higher risk of sudden adverse cardiac events (e.g., sudden death, myocardial infarction) than during periods when they are being less active. However, active people are at less risk than inactive people both during activity and during inactivity. When the risks during activity and at rest are averaged over the whole day, active people have a lower risk.

The risks of sudden adverse cardiac events are greater for those who remain sedentary than for those who increase their regular level of physical activity in a gradual manner. Risks of sudden cardiac adverse events are lower for light- and moderate-intensity activities than for vigorous activities, and likely depend on relative intensity as much or more than absolute intensity.

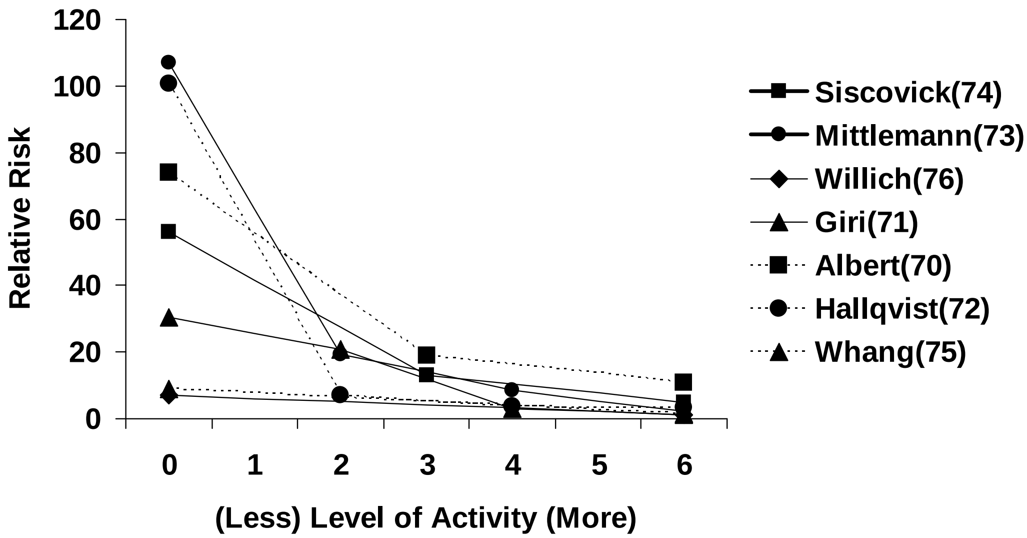
Because cardiovascular risks are more closely associated with intensity of activity than with frequency or duration, common practice in aerobic activity programs is to increase frequency and duration of activity before increasing intensity. Although the safety of specific amounts of increase have not been empirically established, the available scientific literature suggests that adding a small and comfortable amount of light to moderate intensity activity, such as walking, 5 to 15 minutes per session, 2 to 3 times per week, to one's usual activities has a low risk of musculoskeletal injury and no known risk of sudden severe cardiac events.

Current recommendations for physical activity state that asymptomatic men and women who plan prudent increases to their daily physical activities do not need to consult a health care provider before doing so. The incidence of activity-related cardiovascular or musculoskeletal adverse events has not been shown to be reduced by a medical consultation.

Rationale

As shown elsewhere in this report (see ***Part G. Section 1: All-Cause Mortality*** and ***Part G. Section 2: Cardiorespiratory Health),*** the cardiovascular benefits of regular physical activity for adults outweigh the associated cardiovascular risks, including the risk of sudden cardiac death and myocardial infarction. In addition, 7 epidemiologic studies published between 1984 and 2006 compared the incidence of sudden adverse cardiac events (i.e., cardiac arrest, sudden death, myocardial infarction) during or shortly after vigorous physical activity between less and more active people (Table G10.A3, which summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/). These studies uniformly reported a lower risk per minute of activity for more active people (Figure G10.4) (70-76).

Figure G10.4. Risk of Sudden Adverse Cardiac Event by Level of Activity



Relative Risk=risk per minute of vigorous activity/risk per minute of not vigorous activity
Definitions of level of activity differ across studies

Figure G10.4. Data Points

Study	Level of Activity 0	Level of Activity 1	Level of Activity 2	Level of Activity 3	Level of Activity 4	Level of Activity 5	Level of Activity 6
Siscovick (74)	56	–	–	13	–	–	5
Mittlemann (73)	107	–	19.4	–	8.6	–	2.4
Willich (76)	6.9	–	–	–	–	–	1.3
Giri (71)	30.5	–	20.9	–	2.9	–	1.2
Albert (70)	74.1	–	–	18.9	–	–	10.9
Hallqvist (72)	100.7	–	6.9	–	3.7	–	3.3
Whang (75)	9	–	–	–	–	–	1.5

Two of the studies also report that the absolute rate of sudden death during vigorous physical activity is quite low (70;75).

In all 7 studies, the overall relative risk of vigorous physical activity was elevated (median 4.9). When stratified by usual level of activity, the median relative risk of adverse event during vigorous physical activity was 56 for the least active group in each study compared with a median relative risk of 2.4 for the most active group.

Six of the studies used case-crossover methodology, a technique useful for examining a brief period of risk related to a brief exposure, in which cases serve as their own control. One study (74) was exclusively a case control study; others augmented the case-crossover design with case-control designs (72;76) or performed the case-crossover analysis within a cohort design (70;75). In 6 of the studies, vigorous physical activity was defined as requiring 6 or more METs; in one it was defined as 5 or more METs (75).

All the studies included middle to older aged adults and, therefore, provide no information about populations younger than 40 years of age. Two studies included only males (70;74), one included only females (75), and in the remainder, 23% to 32% of the participants were female. One study reported that 90% of subjects were white (71); others provided no information about the racial composition of the study samples. Three studies excluded persons with cardiovascular disease or other “major” chronic conditions (70;74;75).

Three studies provided information about the weighted or average risk of sudden adverse cardiac events in addition to the relative risk per minute of vigorous activity. Because active people are active for more minutes than are inactive people, it is possible that the average risk of sudden adverse cardiac events might be higher for them. Two studies reported that the average risk of events declines with higher levels of regular physical activity (74;75); one reported no difference (70). Data from one of the studies shows that even though the risk of the active person during activity exceeds the average risk of an inactive person, the average risk of an active person over a 24-hour period is less (Figure G10.5) (74;77). In the words of one investigator, to speak of sudden death as a risk of exercise is misleading. Sudden death is, more accurately, a risk of inactivity (78).

Two studies estimated the absolute incidence of sudden cardiac deaths, reporting $3.5*10^{-6}$ and $3*10^{-8}$ per hour of vigorous activity for men (70) and women (75), respectively, confirming the low incidence of such adverse events.

What Do These Findings Imply for Light- or Moderate-Intensity Physical Activity?

The previously described studies investigated risks associated with vigorous physical activity (generally 6 or more METs). The cardiovascular risks of light or moderate intensity physical activity are expected to be less, but quantitative estimates are rare. One of the studies described above (76) reported the relative risk of mild-to-moderate activity to be 0.9, essentially equivalent to the relative risk of sedentary activity (1.1) and sleep (0.8). Among Finnish men, the risk of sudden cardiovascular death during “non-strenuous” activity was reported to be about one-third the risk during “strenuous” activity (79). In an evaluation of an intervention promoting walking among healthy sedentary persons aged 70 to 89 years, abnormal heart rhythms were more common among subjects in the intervention arm than among control subjects (64). The intervention encouraged walking at moderate intensity with a goal of at least 150 minutes per week.

Figure G10.5. Risk of Cardiac Arrest During Vigorous Activity and at Rest by Usual Level of Activity

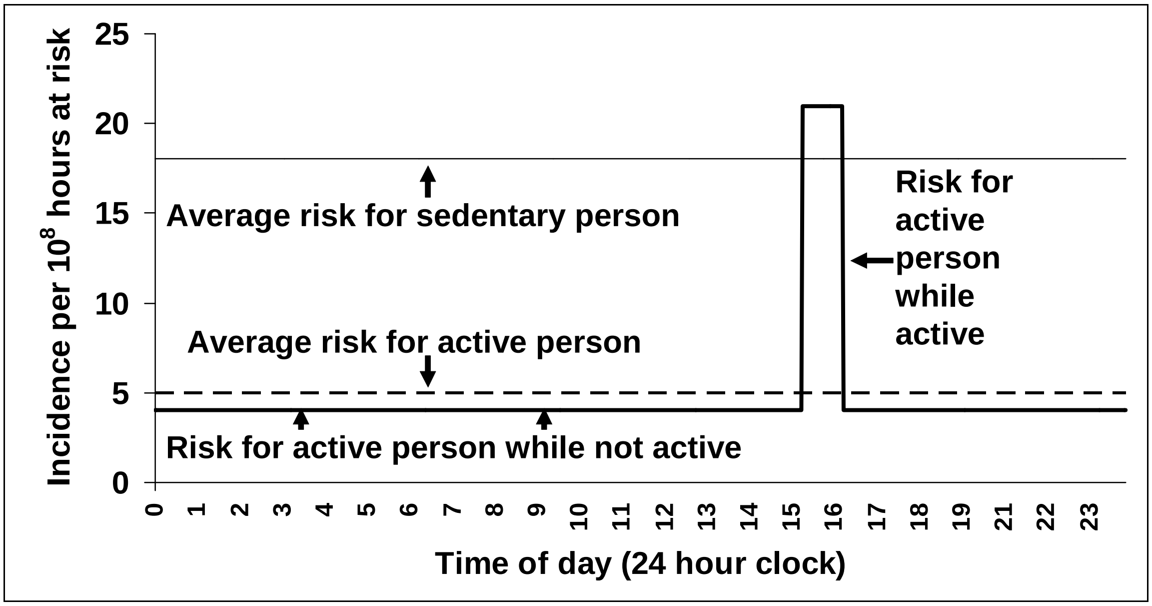


Figure G10.5. Data Points

Risk by Level of Activity	Incidence of Cardiac Arrest per 10^8 Hours at Risk
Average risk for sedentary person	18
Average risk for active person	5
Risk for active person when not active	4
Risk for active person when active	21

In summary, information about the activity-related cardiovascular risks of moderate or light activity is limited. Available information is consistent with the expectation that the risks are substantially lower than those associated with vigorous activity. One would also expect the risks to be lower for regularly active persons than sedentary persons, as is the case for vigorous physical activity.

What Do These Findings Imply for Activities of Low Absolute but High Relative (Perceived) Intensity?

These 7 studies examined the risks of activities requiring 6 or more METs (in one case, 5 or more METs). Individuals, however, vary in their capacity to perform activities with high energy requirements. In general, capacity is lower for females than males, declines with age, appears to be influenced by genetics, and is modulated by routine physical activity practices. Activities requiring about 6 METs of energy expenditure generally cannot be done by persons 80 years and older, are perceived as hard to very hard for middle aged and older adults, and as moderately intense for young adults (Table G10.4) (80).

Table G10.4. Absolute Intensity by Age Group and Relative (Perceived) Intensity (80)

Relative (Perceived) Intensity	Absolute Intensity (METs) in Healthy Adults Young (20-39 yr)	Absolute Intensity (METs) in Healthy Adults Middle-Aged (40-64 yr)	Absolute Intensity (METs) in Healthy Adults Older Adults (65-79 yr)	Absolute Intensity (METs) in Healthy Adults Oldest Adults (80+ yr)
Very light	<2.4	<2.0	<1.6	≤1.0
Light	2.4-4.7	2.0-3.9	1.6-3.1	1.1-1.9
Moderate	4.8-7.1	4.0-5.9	3.2-4.7	2.0-2.9
Hard	7.2-10.1	6.0-8.4	4.8-6.7	3.0-4.25
Very hard	≥10.2	≥8.5	≥6.8	≥4.25
Maximal	12.0	10.0	8.0	5.0

MET, metabolic equivalent

To the extent that regular physical activity habits influence these general findings, sedentary persons would find the relative intensity of any activity of 6 METs to be higher than indicated by the table and very active persons would find it to be lower. As a result, when performing the same activity, sedentary individuals experience more cardiovascular stress than do active individuals. This, plus the fact that sedentary individuals are probably more likely to have atherosclerotic coronary arteries, helps explain the elevated risk of sudden adverse cardiac events among sedentary individuals during activity defined as vigorous on an absolute scale.

As a result, perceived intensity or level of exertion may be a better indicator of cardiovascular stress than absolute intensity (5). Several scales of perceived exertion have been developed and are in use. The terms used to describe a mid-range of exertion are “fairly light” to “somewhat hard,” “weak” to “moderate,” or “light.” Available evidence suggests that individuals striving to be more physically active should, especially initially, adjust their perceived effort to this light to moderate level. They should not strive to perform at an arbitrary absolute level, such as walking at a set pace of 3.5 or 4 miles per hour.

What Do These Findings Imply for Persons Interested in Increasing the Amount or Intensity of Their Physical Activity Practices?

These findings, as did the research findings for the risk of musculoskeletal injuries, indicate that the sedentary persons are most in need of increasing their physical activity level and are those who are also at greatest risk of adverse events when performing activities. The risk of sudden adverse cardiac event is inversely related to the amount of vigorous physical activity (Figure G10.6) (77).

Figure G10.6. Risk of Cardiac Arrest During Activity and at Rest by Usual Level of Activity

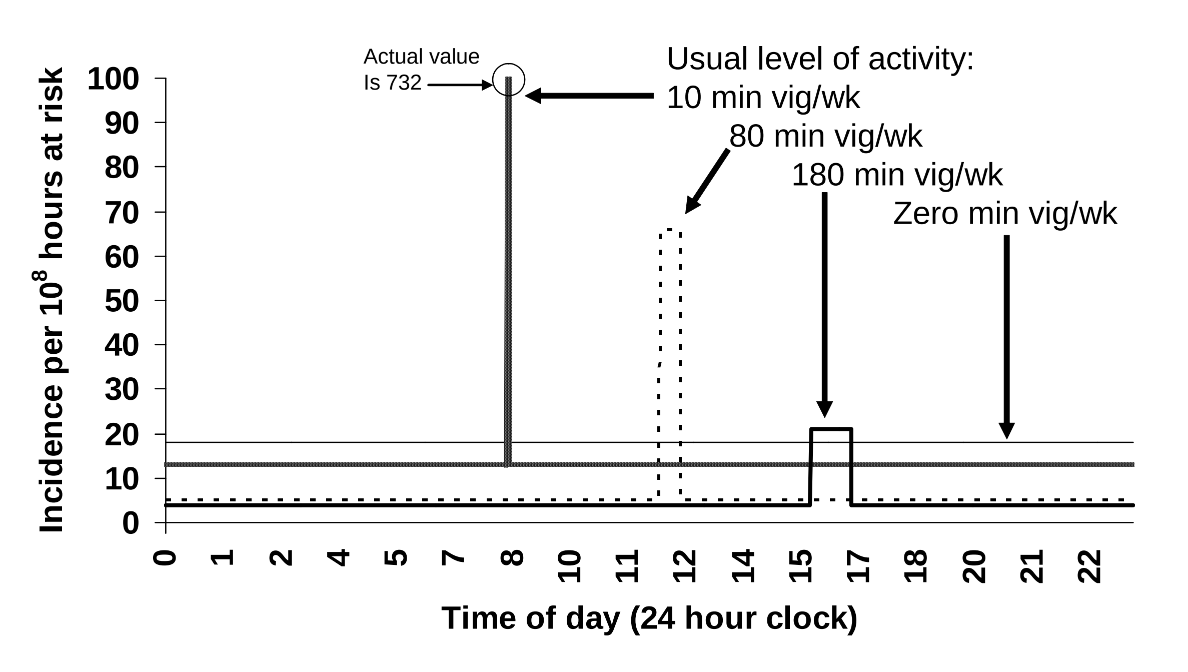


Figure G10.6. Data Points

Risk by Level of Activity	Incidence of Cardiac Arrest per 10^8 Hours at Risk
Risk for person with no minutes per week of vigorous physical activity	18
Risk for person with 10 minutes per week of vigorous physical activity while sedentary	13
Risk for person with 10 minutes per week of vigorous physical activity while vigorously active	732
Risk for person with 80 minutes per week of vigorous physical activity while sedentary	5
Risk for person with 80 minutes per week of vigorous physical activity while vigorously active	66
Risk for person with 180 minutes per week of vigorous physical activity while sedentary	4
Risk for person with 180 minutes per week of vigorous physical activity while vigorously active	21

The risks of remaining sedentary, however, are greater than the risks of becoming active, especially if increases in activity are prudent. For cardiovascular risk, the intensity of the activity is of greatest concern (81). Because the cardiovascular risks are more closely associated with intensity than with frequency or duration, common practice in aerobic activity programs is to increase frequency and duration of activity before increasing intensity (52). Although the safest method of increasing one's physical activity has not been empirically established, drawing upon the principle of overload and adaptation of exercise science and the experience of supervisors of cardiac rehabilitation programs, walking so that the perceived intensity is in the light to moderate range (5) until one is able to walk 20 to 30 minutes per session for several weeks is an acceptable and safe way to begin. For older adults who are increasing their physical activity level, cardiovascular adaptation to an augmented activity regimen may take as long as 20 weeks or more (82), suggesting that activity levels should be increased at monthly rather than weekly intervals.

Are There Any Types of Heart Problems or Other Medical Problems for Which Vigorous Physical Activity, Even by Regularly Active Individuals, Poses More Risk Than Benefit?

Unlike atherosclerotic coronary artery disease, for which regular (including vigorous) physical activity is beneficial, hypertrophic cardiomyopathy, anomalous coronary arteries, long QT syndrome, Marfan syndrome, and other congenital cardiac anomalies are not benefited by regular, especially vigorous, physical activity. The risks posed by these conditions rises with the intensity of activity performed. Therefore, although regular moderate-intensity physical activity may benefit individuals with these conditions by reducing the risk of atherosclerotic disease, diabetes, obesity, and other conditions related to under activity, vigorous physical should be avoided (81). People with sickle trait, a trait more common among African Americans than other groups, are more likely to suffer rhabdomyolysis and sudden death during exercise than those who do not carry the trait (83;84).

How Do These Studies Apply to Children, Adolescents, and Young Adults?

The studies reviewed for this chapter do not apply because children, adolescents, and young adults rarely have atherosclerotic heart disease. In contrast to adults for whom activity-related sudden adverse cardiac events is almost always due to atherosclerotic coronary artery disease, activity-related sudden adverse cardiac events among youth are primarily due to congenital abnormalities.

Nontraumatic sports deaths (e.g., cardiovascular, hyperthermia, rhabdomyolysis, and sickle cell trait) in high school and college athletes are uncommon, with incidence rates of about 7.5 per million per year among male athletes and 1.3 per million per year among female athletes (85). About 75% of the deaths are due to cardiovascular causes. Because these deaths are so uncommon, the evaluation of various screening mechanisms is difficult (86;87).

For children, adolescents, and young adults (ages 1 to 24 years) the U.S. Preventive Services Task Force (USPSTF) recommends "counseling patients to incorporate regular physical activity into their daily routines" (88). However, the USPSTF recommends against routine electrocardiographic screening as part of the periodic or pre-participation sports physical exam (88). Current recommendations of the American Heart Association are that high school and collegiate athletes should be evaluated by a "healthcare worker with the requisite training, medical skills, and background," and that the evaluation "should include a complete medical history and physical examination" including blood pressure measurement (86). For a detailed discussion of issues related to physical activity and youth, see ***Part G. Section 9: Youth.***

Is a Health Care Evaluation Necessary Before Augmenting One's Current Physical Activity Practices?

Evidence that persons who consult with a health care provider before increasing their physical activity receive more benefits or suffer fewer adverse effects than persons who do not is not available. Also unknown is the extent to which official recommendations to seek medical advice before augmenting one's regular physical activity practices may reduce participation in regular moderate physical activity by implying that being active may be less safe and provide fewer benefits than being inactive (78).

Recent recommendations have suggested that asymptomatic men and women who plan sensible increases in light to moderate physical activity do not need to consult a health care provider before doing so (36;81). Others, generally concurring with the safety of small increases in light to moderate activity, have recommended that "previously inactive" men aged 40 years and older, women age 50 years and older, and people who have chronic disease or risk factors for chronic disease should consult a physician before starting a vigorous activity program (23;89;90).

These two perspectives, one calling attention to the safety of small increases and the other to the risks of large increases, are consistent with the findings of this chapter. A substantial increase in physical activity over one's customary routine — either as a single episode, as shown in the studies of acute adverse cardiac events, or as a more sustained program, as for the military recruits — is associated with higher risks of adverse events than are smaller and more gradual increases. The risk is associated with the magnitude of the relative discrepancy between the usual level and new level of activity rather than with other personal characteristics. Adding a small and comfortable amount of walking, such as 5 to 15 minutes 2 to 3 times per week, to one's usual daily activities has a low risk of musculoskeletal injury and no known risk of sudden severe cardiac events. Choosing a comfortable level of effort, initially increasing only frequency and duration of activities, and allowing adequate time for adaptation to each new level of activity minimizes the already low risk of injuries or other problems.

Question 4. What General Factors Influence the Risks of Musculoskeletal Injury and Other Adverse Events Related to Physical Activity?

Conclusions

In addition to the type, dose, and relative size of increase of physical activity, the risk of musculoskeletal and other adverse events is related to several key factors:

- Demographic and personal characteristics. Low levels of physical activity or fitness and previous musculoskeletal injuries are two of the most important individual-level risk factors for injuries and other adverse events.
- Quality and appropriateness of equipment, including protective gear. Proper equipment (e.g., bicycle helmets) reduces risk.
- Safety of the environment. Safe places for children to play, structures that limit vehicular speed, and mechanisms that keep pedestrians and bicyclists separated from motor vehicles reduce the risk of activity-associated injuries. Fear of crime is a barrier to physical activity although no evidence exists that people are at greater risk of crime during periods of activity than periods of inactivity.
- Prudent attention to each of these components of activity-related risk can reduce the rate of adverse events and enlarge the benefit to risk ratio.

Rationale

Demographic and Personal Characteristics

Demographic and personal characteristics influence the type and amount of physical activity people do and, thereby, influence the risk of injury. This section, however, is concerned not with whether these characteristics influence the choice of activity but whether they influence directly the risk of injury. Two types of questions may be of interest. First, do people with different characteristics (e.g., old or young) but doing the same amount and type of activity have the same risk of activity-related injury? Second, do people with the same characteristic (e.g., overweight) but different activity habits (i.e., active or inactive) have the same risk of injuries from all causes? Information is not always available to address both questions.

Age

Are older and younger people at the same risk of activity-related injury? One would expect the risk of injuries and other adverse events to increase with age. The physiologic changes of aging, such as the decline in maximal heart rate and cardiac output, decline in connective tissue elasticity, decline in balance, and fall in the speed of reflexes, all would appear to make older people more easily afflicted by physical activity-associated adverse events.

Surprisingly few studies have actually examined the topic. Studies of military recruits report higher injury rates among older recruits even though the oldest recruits are in their mid to upper 20s (35;91). Surveys of active adults of all ages, however, report lower injury rates among older than younger persons (9;12;14;17;92). This surprising finding presumably arises from a confounding of age with exposure — the fact that older individuals cannot perform and do not attempt to perform at levels comparable to younger persons.

Are active and inactive people of similar age equally likely to be injured? The incidence of injuries from all causes (not only activity-related injuries) is a function of both age and level of physical activity. Among younger people, physically active people report more injuries requiring medical attention than inactive people; whereas among older people inactive people report more injuries (Table G10.5) (9).

Table G10.5. Annual Incidence* of Self-Reported Injury Requiring Medical Advice by Age Group and Leisure-Time Physical Activity Level (9)

Age Group (years)	Overall	Active†	Insufficiently‡ Active	Inactive§
18-24	116.6	126.4	132.5	96.5
25-34	97.3	112.7	85.1	91.8
35-44	87.0	93.0	75.5	91.2
45-64	76.4	72.6	76.5	81.6
65+	68.1	60.6	56.1	74.4

* Incidence per 1,000 population
† Meet current physical activity recommendations
‡ Report some leisure-time light-moderate or vigorous physical activity but do not meet current recommendations
§ Report no leisure-time light-moderate or vigorous physical activity

Are children and adolescents more susceptible to overuse injuries? The growing child or adolescent may have an increased susceptibility to certain repetitive stress injuries such as traction apophysitis (e.g., Osgood-Schlatter disease), injuries to the immature spine, or others (93). These established developmentally-linked injuries and the growth of organized competitive sports for youth and the sometimes prolonged and intensive training attendant with successful participation in those sports has raised concern about "the sensibility and safety of high-level athletics for any young person" (94). Little empirical evidence is available on which to assess the magnitude and risk factors for the problem. Drawing upon expert opinion and clinical experience, recommendations, the American Academy of Pediatrics makes the following recommendations (94;95):

- Participation in sports should be at a level consistent with the child's abilities and interests;
- Athletes should take off 1 to 2 days per week and 2 to 3 months per year from any specific sport;
- Athletes should participate on only 1 team per season;
- Athletes should not increase their training load by more than 10% per week;
- Coaches, trainers, and parents should be alert to the possibility of overuse injuries;
- Treatment recommendations should include alternatives to "rest only" programs because they are not likely to be followed; and
- Fun, sportsmanship, skill acquisition, and safety should be emphasized.

Although overuse injuries may be a concern for some children and youth, for the large majority of children insufficient physical activity is a greater concern than too much activity (See ***Part G. Section 9: Youth*** for a detailed discussion of this topic).

In summary, for a specific dose of activity older people are more likely than younger people to be injured. In practice, however, older people consciously or unconsciously appear to moderate their physical activity so that they become injured less frequently than do younger persons. When compared to inactive individuals, physically active younger persons are injured more frequently than inactive younger persons whereas physically active older persons are injured less frequently than inactive older persons.

Sex

Currently available research suggests that, aside from stress fractures and injuries to the anterior cruciate ligament of the knee, which are more common in females (51;96;97), males and females appear to be equally susceptible to activity-related injuries (34;37;98-100). In population surveys, males are more likely to report having been injured than females (34), but they are also more likely to report being physically active (101). In military studies in which males and females partake of the same dose of activity, females are about twice as likely as males to be injured (10;102), but they, as a group, are also less physically fit than males at the beginning of basic training (102;103). When injury rates are adjusted for initial physical fitness, the risks of injury for females and males are equivalent (98;102;103). This is consistent with findings from college athletes in which sport- and sex-specific injury rates are similar for males and females (99;100).

Race and Ethnicity

The influence of race and ethnicity on activity-related musculoskeletal injuries has been uncommonly reported. Most studies of military recruits report no differences among race and ethnic groups in the incidence of musculoskeletal injuries (35;40-42). In one study, the incidence of stress fractures was higher for whites than blacks (104). However, certain health conditions that are more common in one race or ethnic group may influence injury or illness rates. For instance, people with sickle trait, a trait more common among African Americans than other groups, are more likely to suffer rhabdomyolysis and sudden death during exercise than those who do not carry the trait (83;84).

Anatomical Characteristics

The few studies that have examined anatomical factors suggest that self-reported leg-length discrepancies (105), and clinically measured high arches (106), genu valgum (knock knees) (107) and high quadriceps angle (107;108) are associated with higher risks of musculoskeletal injuries than is the case for persons who do not have these anatomical characteristics.

Behavioral Factors

Fitness and physical activity. Low levels of physical fitness and physical activity are among the most important risk factors for musculoskeletal injuries and sudden adverse cardiac events. Please see the detailed discussion earlier in this chapter on the relationship between physical activity, injuries, and levels of physical fitness.

Stretching. Persons with high or low levels of flexibility appear to be more likely to be injured than persons in the middle range of flexibility (35;40). However, stretching, per se, has not been shown to be effective for either injury prevention or improved performance (109). Some evidence indicates that stretching combined with other actions, including warm up, strength training, or general conditioning, prevents injuries (109).

Warming up and cooling down. Warming up and cooling down before and after exercising are commonly recommended to prevent injuries and adverse cardiac events. Although evidence is limited, various combinations of warm-up, strength training, conditioning, and stretching are associated with lower rates of musculoskeletal injuries (109).

Following a survey of major cardiovascular complications during exercise training at cardiac rehabilitation programs, which reported that 44 (72%) of 61 adverse events occurred near the beginning or at the very end of the session (110), careful warming up and cooling down have become standard practice in cardiac rehabilitation programs. Evidence consistent with myocardial ischemia during sudden strenuous exercise without warm-up has been noted in some studies (111-113) but not others (114). In the period immediately after strenuous exercise catecholamine blood levels are elevated, posing potential risk, especially for persons with coronary artery disease (115).

Despite limited evidence of helpfulness, guidelines recommend 10 to 20 minutes of stretching and progressive warm-up activity before the main activity session (116). Following the main activity, 10 to 20 minutes of gradually diminishing activity is recommended.

Existing Health and Medical Conditions and Behaviors

Tobacco use. Cigarette smoking (40;45;117) and smokeless tobacco use (91) have been associated with higher rates of musculoskeletal injuries among military recruits undergoing basic training. The associations are strong (2- to 3-fold), are directly related to the usual number of cigarettes smoked, and persist after controlling for other risk factors, such as physical fitness.

Prior musculoskeletal injuries. Prior injury is one of the most consistently reported and strongest risk factors for future injury, with the risk generally reported to be about two-fold (10;29;34;35;41;47;108;118;119). Reinjury may occur because the original injury has not healed or the wound and surrounding structures have been inadequately rehabilitated (34), or because the primary risk factor has not been modified (e.g., structural or training defect). Prior or current injury is one of the most common barriers to participation in regular physical activity at recommended levels (1-4).

Pregnancy. Current recommendations state that participation in a wide range of aerobic and recreational activities of moderate intensity is safe for healthy pregnant women with uncomplicated pregnancies (120;121). Given the many years, however, of clinical and public health efforts to promote and provide appropriate medical care for pregnant women, surprisingly little is considered firmly established about the benefits and risks to pregnant women and their fetuses of physical activity. A systematic review by Kramer and McDonald (122) noted that insufficient data from small clinical trials whose methodological quality was not high made it difficult to infer important risks or benefits of physical activity for the woman or the fetus. Potential benefits specific to pregnancy, such as preventing gestational diabetes and maternal weight control and promoting maternal fitness, easier and less painful deliveries, and improved mental health, have been suggested by epidemiologic studies but are not yet firmly established. (See ***Part G. Section 11. Understudied Populations*** for a detailed discussion of physical activity and pregnant women.) Prenatal medical evaluation is recommended for every pregnant woman to be sure that she does not have one of the rare but absolute contraindications for physical activity during pregnancy (120) and to develop an appropriate physical activity program during the pregnancy and postpartum period.

Overweight and obesity. Studies of activity-related injuries among military recruits, runners, and other active people report varied findings. Some report no association (3;28) between weight status and risk of activity-related injuries, and others report elevated rates among those with higher body mass index (BMI) (118;123). Still others report elevated rates among military personnel with lower and higher BMI (39;45) compared to those in the middle range.

Given the mixed findings and the fact that these groups contain few overweight and almost no obese individuals, the results from these studies are difficult to apply to overweight and obese individuals. For injuries of any cause, not just activity-related injuries, population-wide studies indicate that overweight and obese individuals are more likely than persons of normal weight to report a medically attended injury (Table G10.6) (9;124).

Table G10.6. Rate or Odds Ratio of Medically Attended Injury of Any Cause, by BMI Category

Subjects of 2000-2002 NHIS (9) BMI Range	Subjects of 2000-2002 NHIS (9) Rate Ratio	Subjects of 1999-2002 MEPS (124) BMI Range	Subjects of 1999-2002 MEPS (124) Odds Ratio
–	–	<18.5	0.97
<25.0	1.00	18.5-24.9	1.00
25-29.9	1.09	25.0-29.9	1.15
≥30	1.17	30.0-34.9	1.24
–	–	35.0-39.9	1.26
–	–	≥40.0	1.48

BMI, body mass index; NHIS, National Health Interview Survey; MEPS, Medical Expenditure Panel Survey

Another way to look at this issue is to ask whether active and inactive overweight people are at equal risk of activity-related injuries. One study has found that obese persons who are regularly active have been reported to be nearly 15% less likely to be injured from any cause than inactive obese persons (9).

Acute upper respiratory tract infections (URTI). Although evidence is not yet abundant, current scientific literature suggests that people who are physically active at currently recommended levels suffer fewer URTI than either sedentary individuals or athletes participating in intense exercise training.

Recent studies of children (125), adolescents (126), adults (127), postmenopausal women (128), and elderly adults (129) all report fewer URTI among more active individuals than among less active. Another study among the elderly reported no difference in the incidence of URTI but less fever and activity restriction among active than inactive persons (130).

In contrast, recent studies that include persons participating in intense exercise training such as elite athletes report either no difference between groups (131;132) or the highest rates of URTI among the athletes at the highest level of competition (133-135). In studies with elite athletes the curves showing infection rates across groups display a "J" shaped dose-response curve, with the inactive participants having slightly elevated rates, moderately active individuals the lowest rates, and the extremely active participants the highest rates of URTI.

Engaging in moderately intense physical activity during a URTI appears to be safe. Vigorous activity is discouraged, especially if evidence of systemic involvement, such as fever, muscle aches, swollen lymph nodes, or extreme fatigue, exists (136;137).

Chronic diseases. For many chronic diseases, including the most prevalent conditions such as atherosclerotic heart disease, diabetes, arthritis, or chronic lung disease, participation in an appropriately designed physical activity program is therapeutically beneficial (138-141). Review and discussion of the evidence pertaining to physical activity as a treatment for specific conditions is beyond the scope of this chapter. For some severe conditions physical activity may be contraindicated or severely restricted; the Canadian Society for Exercise Physiology supported by Health Canada has proposed a list of such conditions (142).

Current recommendations state that most people with a chronic disease can safely add several minutes of walking or other light to moderate intensity activity to their everyday activities. Persons with cardiovascular disease, diabetes, or other active chronic conditions who want to begin engaging in **vigorous** physical activity and who have not already developed a physical activity plan with their health care provider may wish do so (36;81). Appropriately designed physical activity regimens for individuals with a wide range of disabilities has been shown to be safe and effective (see ***Part G. Section 11: Understudied Populations,*** for a detailed discussion of physical activity and people with disabilities).

Quality and Appropriateness of Equipment

Shoes

Comfortable shoes that fit properly are associated with less foot pain, fewer blisters and ulcers, and lower risk of future development of foot problems than are poorly fitting shoes. This is true for all people, regardless of activity. Proper footwear is especially important for persons with diabetes or other conditions that interfere with circulation or sensation of the feet. Recent reviews indicate that shock absorbing inserts reduce the incidence of stress fractures in military personnel (143) and that external ankle supports reduce the incidence of ankle sprains during high-risk activities such as basketball or soccer (144). The value of pronation control and cushioning in running shoes, and lateral stability, torsion control, traction, and cushioning in court shoes is generally assumed despite limited scientific support (145). Comfort is one of the, if not the, most important aspects of a sport shoe.

Clothing

For pedestrians and cyclists, the use of red, yellow, and orange fluorescent materials improves recognition by drivers of vehicles, and lamps, flashing lights, and reflective materials help at night (146). However, neither the use of fluorescent materials during the day nor lights or reflective gear at night has been shown to reduce collisions or injuries. Proper clothing also reduces the risk of injury from cold or hot temperatures (see section on Climate, below) (147;148).

Bicycle Helmets

The protective effects of bicycle helmets have been firmly established, and their use is recommended for commuting, recreational, and competitive bicycling. A recent meta-analysis estimated that the use of bicycle helmets reduced the risk of death by nearly 75%, risk of head injury and brain injury by about 60%, and risk of facial injury about 50% (149). An estimated 107,000 unnecessary bicycle-related head injuries, $81 million in direct medical costs, and $2.3 billion in indirect health costs in 1997 resulted from bicyclists in the United States not wearing helmets (150).

Other Gear and Equipment

Proper protective equipment has been shown to reduce the rate of specific types of injuries in a variety of activities. Breakaway bases and reduced-impact balls in baseball and softball, mouth guards in basketball, helmets in football, full face shields in hockey, wrist guards in in-line skating, binding adjustments in skiing, and other protective gear have been shown to reduce injuries (151).

Safety of the Environment

Physical activity is performed in many different environments, including outdoor and indoor facilities, urban and rural settings, and hot and cold temperatures. Many features of these environments influence the risk of injuries. A common environment for physical activities such as walking, gardening, bicycling, and playing is residential neighborhoods. Two-thirds (66%) of respondents to a recent survey reported their neighborhood as a site for physical activity (152). The next paragraphs pertain to risk factors within residential neighborhoods, namely, traffic, crime, air pollution, and weather.

Safety from Traffic and Crime

Traffic safety in neighborhoods. Injury rates of pedestrians and cyclists in the United States are 2- to 4-fold higher than in Germany and the Netherlands (153). Two important features of safe walking and biking are lower traffic speed and separation from traffic. Neighborhoods can be modified to reduce traffic speed and to assure separation between pedestrians, cyclists, and motor vehicles. Mechanisms to slow traffic, sometimes referred to as traffic calming, include 1) vertical deflections (e.g., speed bumps), 2) horizontal deflections (e.g., bends), 3) road narrowing, and 4) medians, four-way stops, and small roundabouts (154-156). Mechanisms to separate pedestrians and cyclists from traffic include installation and maintenance of 1) sidewalks and bicycle lanes, 2) pedestrian over- and underpasses, and 3) fences or parkways between sidewalks and streets (155;157). Methods of reducing the risk at crossings — areas shared by pedestrians, bicyclists, and motor vehicles — include the installation of traffic signals, pedestrian prompting devices (e.g., signs), in pavement flashing lights to warn drivers when pedestrians are present, traffic signals with exclusive walk signal phasing, refuge islands, raised medians, and improved nighttime lighting (155;158;159). Less is known about creating safe environments for bicycling than for walking (160).

Safe walking to school. When asked why their children do not walk to school, 30% of parents cite traffic safety concerns and 12% cite fear of crime (161). Special programs have been implemented specifically to improve the safety from both traffic and crime for children going to and from school. The Federal Highway Administration's *Safe Routes to School* provides funding to states for educational and environmental change to encourage walking and biking to school (162). An online newsletter reports that pedestrian injuries were not increased in spite of more children walking and biking to school with Safe Routes to School programs (163).

Crime reduction. Fear of violent crime is a barrier to participation in physically active pursuits. Adults, adolescents, and children who live in neighborhoods perceived to be unsafe have been shown to be less physically active compared to those living in areas perceived to be safe (164;165). No evidence exists that people are at greater risk of violent crime (e.g., assault, rape) during periods of activity than periods of inactivity. When considering walking, running, or other physical activities in an unfamiliar place, crimes are less likely to occur in places that are well lit, where other people are present, and that are lacking signs of neglect such as litter, graffiti, empty buildings, buildings in disrepair (e.g., broken windows) (154).

Safety tips to protect from traffic and crime are available (Table G10.7) (166). They have face-validity although few have empirical support.

Table G10.7. Safety Tips to Avoid Becoming Victim of Crime, Avoid Traffic Injuries, or Minimize the Effects of Either*

1. Carry identification
2. Bring a partner, human or canine
3. In unfamiliar areas, inquire about safety
4. Leave word where you are going and when you'll be back
5. Stay alert and aware of surroundings
6. Don't wear headphones
7. Avoid unlit areas
8. Avoid unpopulated areas and deserted streets
9. Ignore verbal harassment
10. Carry cell phone or money to make a phone call
11. Carry a noisemaker
12. Contact police immediately if something happens

* Source: Adapted from Road Runners Club of America (2007)

Air Pollution

The balance between the risks and benefits of being physically active in air polluted at levels commonly experienced in the United States is not established. Air pollution is a complex mixture of gases, liquids, and particulate matter. Levels and constituents of air pollution vary among and within cities. Air pollution is generally most intense near busy roadways and industrial sites. It can be indoors or outdoors depending on the type and origin of the pollutants.

Both long- and short-term exposure to air pollution have been shown to increase all-cause, cardiovascular, and pulmonary mortality, hospital admissions, emergency room visits, and symptoms (167;168). The Environmental Protection Agency has developed an Air Quality Index and, depending upon the value of the index, individuals may be advised to reduce or avoid “prolonged or heavy exertion” out of doors (169).

Physical activity increases the volume of inhaled air and exposure to airborne toxins and allergens (170). Elevated levels of air pollution are associated with reductions in maximal exercise performance (171;172). Exercisers have been warned to avoid exercising near heavy traffic and industrial sites, especially during rush hour (170;173). Such recommendations may be reasonable for individuals who can easily modify the location or time for exercise. However, they may be a barrier to regular physical activity for people with less flexible daily demands. In addition, they take into account only short-term adverse effects of physical activity in polluted air. The long-term benefits of regular physical activity in polluted air may outweigh the short-term risks. Lower mortality rates among more active than less active individuals in a polluted industrial community have been reported (174). Regular physical activity in a polluted environment may ameliorate the adverse effects of pollution just as it reduces the adverse health effects of obesity and diabetes.

No evidence exists that physical activity in air polluted to the current levels of American cities negates the benefits of physical activity. From a health perspective, it would be preferable to reduce air pollution than reduce the already low physical activity levels of Americans.

Temperature Extremes

It is safe for healthy people to be physically active in a wide range of normally encountered temperatures. Proper clothing is important. Acclimatization — physiologic adaptation (e.g., greater volume and less concentrated sweat) to repeated exposures to warm weather — occurs over several weeks and increases the safety warm weather activity. A protective acclimatization to very cold weather does not occur. Specific guidelines regarding activity in extremely cold (148) and hot (147) conditions have been published, as have guidelines for maintaining adequate hydration in these settings (175).

Question 5. Do the Benefits of Regular Physical Activity Outweigh the Risks?

Conclusions

The benefits of physical activity outweigh the risks.

Rationale

Outcomes that encompass a broad spectrum of medical maladies — such as all-cause mortality, functional health, or medical expenditures — sum both positive and negative effects of physical activity. All-cause mortality, for example, encompasses deaths caused and prevented by activity; and medical expenditures include costs incurred and avoided because of physical activity.

Physically active people have lower all-cause mortality rates, higher levels of functional health, and lower medical expenditures. (See ***Part G. Section 1: All-Cause Mortality*** and ***Part G. Section 6: Functional Health.***) Studies of the influence of physical activity on medical expenditures consistently report lower costs for active individuals when compared with inactive individuals. The savings may be lower or even absent for younger persons, but for adults and older adults physical activity is associated with lower medical costs. These medical expenditures include costs associated with adverse effects and, therefore, indicate an overall benefit from participation in regular physical activity.

Are Medical Expenditures Lower for Physically Active People Than for Inactive People?

Studies of the relationship between medical expenditures and physical activity generally are of two types: direct comparisons of the expenditures of more and less active people, and estimates of the excess costs incurred by inactive people because they are more likely than active people to develop certain conditions such as heart disease, diabetes, or colon cancer.

Direct Comparisons

Eight studies published in the last decade have compared direct medical expenditures for active and inactive individuals who are members of the same group or population, such as employees of a company, enrollees in a health plan, or respondents to national surveys (see Table G10.8 below. Table G10.A4, which also summarizes these studies, can be accessed at http://www.health.gov/paguidelines/report/) (176-183). All report lower medical costs for active persons. For 7 studies, the reductions ranged from 6% to 22% (median, 13%) (176;177;179-183); the eighth reported that costs were reduced 4.7% for each day per week of physical activity (178). All minimized the confounding potential of chronic diseases through exclusion, adjustment, or stratification. All adjusted their findings for age and sex, 6 adjusted for BMI (177-181;183), and 4 adjusted for smoking (177-179;183). Subjects in all of the studies were adults or older adults, with mean ages ranging from 45 years to 75 years.

Table G10.8. Medical Expenditures for Active Versus Inactive Persons

Subjects, Researchers (Citation)	Study Period	Cost Ratios
Members of health plan (178)	1995–1996	4.7% reduction in costs per active day/week
Beneficiaries of National Health Insurance (Japan) (179)	1995–1998	1.00 (ref) walk <31 min/ week 0.97 walk 31-60 min/ week 0.87 walk >60 min/ week
Members of HMO (176)	1997–2000	1.00 (ref) active 0.79 active
Employees of large company (181)	1996–1997	1.00 (ref) 0 times/ week 0.89 1-2 times/ week 0.91 3+ times/ week
Respondents of NHIS and MEPS (182)	1996	1.00 (ref) inactive, no CVD 0.93 active, no CVD 1.00 (ref) inactive, with CVD 0.60 active, with CVD
Respondents of NHIS and NMES with symptoms of depression (183)	1987	1.00 (ref) inactive 0.94 active
Retirees of large company (180)	2001–2002	1.00 (ref) 0 times/ week 0.86 1-3 times/ week 0.78 4+ times/ week
Respondents to NHIS and MEPS with mental disease (177)	1996	1.00 (ref) inactive with mental disease 0.81 active with mental disease

CVD, cardiovascular disease; HMO, health maintenance organization; MEPS, Medical Expenditure Panel Survey; NHIS, National Health Interview Survey; NMES, National Medical Expenditure Survey; ref, reference, value

Estimated Costs

A review summarizing the findings of 10 studies from 6 countries (US-3, Canada-2, Holland-2, Australia-1, Switzerland-1, UK-1) of the annual excess cost (in 2003 $US) per inactive person per year reports a range from -$109 to $1305 (median $172) (184). These studies are done by combining population-wide estimates of physical activity from national surveys with estimates of relative risk of inactivity for specific diseases from observational research studies. Four of the reviewed studies included both direct and indirect costs; 6 included only direct costs. The one study suggesting that inactive individuals have lower medical expenditures stratified the data by age, reporting an annual cost saving of $109 per inactive person aged 15 to 44 years compared with an expense of $87 per inactive person age 45 years and older. Similar methods have been used to develop estimates for 5 States (GA, MN, NY, SC, WA), with annual per capita direct medical costs attributable to physical inactivity ranging from $19 (WA) to $79 (GA) (185).

Overall Summary and Conclusions

The benefits of regular physical activity outweigh the inherent risk of adverse events. Still, adverse events are common and are an impediment to more widespread participation in regular physical activity. Selection of low risk activities and prudent behavior while doing any activity can minimize the frequency and severity of adverse events and maximize the benefits of regular physical activity.

The chapter has focused on musculoskeletal injuries, the most common type of physical-activity associated adverse event, and sudden adverse cardiac events, one of the most severe adverse events. The chapter also has emphasized the key factors of any physical activity program, which are:

- The type of activity;
- The dose of activity as determined by the frequency, duration, and intensity of participation; and
- The rate of progression or change in the dose of activity.

Proper attention to each of these can substantially reduce the risk of adverse events.

The overall conclusions of this chapter can be summarized as follows:

Risk of adverse events and type of activity. Activities with fewer and less forceful contacts with objects or other people have appreciably lower injury rates than collision or contact sports. Walking for exercise, gardening or yard work, bicycling or exercise cycling, dancing, swimming, and golf, already popular in the United States, are activities with the lowest injury rates.

Risk of adverse events and amount of activity. The amount of physical activity is directly related to the risk of musculoskeletal injury. Injury rates at the level of activity commonly recommended (150 minutes per week of moderate intensity activity, or about 500 MET-minutes per week of activity) have been uncommonly documented but appear to be low.

Risk of adverse events and change in amount of activity. The risk of injury is directly related to size of increase in the amount of physical activity performed. A series of small increases in activity each followed by a period of adaptation is expected to cause fewer injuries than larger increases. Adding a small and comfortable amount of walking, such as 5 to 15 minutes 2 to 3 times per week, to one's usual daily activities has a low risk of musculoskeletal injury and no known risk of sudden severe cardiac events. Frequency and duration of aerobic activity should be increased before intensity. Increases in activity level may be made as often as weekly among youth, whereas monthly is more appropriate for older or unfit adults. Attainment of the desired level of activity may require a year or more, especially for elderly, obese, or habitually sedentary individuals.

Risk of sudden adverse cardiac events. The risk of sudden adverse cardiac events (e.g., sudden death, myocardial infarction) are higher during periods of vigorous physical activity than during periods of less intense activity or while at rest for all individuals. However, active people are at less risk than inactive people both during activity and during inactivity. When the risks during activity and at rest are averaged over the whole day, active people have a lower average risk than do inactive people.

The risks of sudden adverse cardiac events are greater for those who remain sedentary than for those who increase their regular level of physical activity, especially if the increase is gradual. Risks of sudden cardiac adverse events are lower for light- and moderate-intensity activities, and likely depend on relative intensity as much or more than absolute intensity. The first changes in an aerobic activity program should be in the frequency and duration rather than the intensity of the activity.

The information about activity-related musculoskeletal and cardiovascular adverse events reviewed in this chapter is consistent with previously made recommendations that asymptomatic men and women who plan prudent increases to their daily physical activities do not need to consult a health care provider before doing so. Evidence that persons who consult with a health care provider before increasing their physical activity receive more benefits or suffer fewer adverse events than persons who do not is not available. Symptomatic persons or those with cardiovascular disease, diabetes, or other active chronic conditions who want to begin engaging in **vigorous** physical activity and who have not already developed a physical activity plan with their health care provider may wish to do so.

Personal characteristics and behaviors associated with higher risks of adverse events. Previous musculoskeletal injuries and low levels of physical activity or fitness are two of the most important individual level risk factors for injuries and other adverse events.

Other factors associated with higher risks of adverse events. Proper equipment, such as bicycle helmets, reduces risk. Neighborhood characteristics that limit vehicular speed and keep pedestrians and bicyclists separated from motor vehicles also reduce the risk of activity-associated injuries. Fear of crime is a barrier to physical activity although there is no evidence that people are at greater risk of crime during periods of activity than periods of inactivity.

Consistency of current findings with previous physical activity recommendations. Adverse events have received relatively little attention in previous physical activity recommendations. When mentioned, however, the statements are consistent with the information presented in this chapter. Several mention the importance of gradual increases in physical activity (22-24;80;186), and several acknowledge the fact that injuries are a potential barrier to participation in physical activity (23;24;80;187).

Research Needs

This review of the literature related to physical activity and adverse events identified a number of questions that would benefit from additional research:

Are active and inactive individuals at equal risk of unintentional injuries? Although physically active individuals are likely to incur more activity-related injuries, limited evidence suggests that they may suffer fewer non-activity-related injuries and, therefore, experience no more and maybe fewer overall injuries than inactive people. The severity of injury and the type and amount of physical activity are likely to be important determinants of the relationship.

What is the appropriate starting dose of activity for individuals who have been inactive? Recommendations to "gradually" increase one's physical activity are commonly made but there is little information to support specific recommendations for an initial dose that will maximize continued participation and minimize adverse events.

What are the appropriate size and frequency of increases in physical activity? Recommendations to increase "gradually" are common but there is little information to support specific recommendations. Size and frequency of increase may also vary by age, length and severity of inactivity, and other factors.

What are the incidence and risk factors for adverse events associated with walking? Current literature suggests that risks may be unrelated to either total volume of walking or intensity (using elevated treadmills). Are these findings substantiated in other settings and populations?

What are the most effective methods of reducing the incidence and severity of adverse events among people who are increasing their physical activity practices? The type, dose, rate of increase, proper protective gear, and safety of the environment are major determinants of injury risk and adherence to an activity regimen. Little is known about the most effective methods of encouraging and enabling the public to safely increase their physical activity practices.

Is there value, and if so for whom, to seeking advice from a health care provider before increasing one's physical activity practices? Although it does not address the preceding question fully, one approach to reducing adverse events among persons who are increasing their physical activity levels has been to suggest that some people (usually those who are older or have one or more chronic conditions) should receive permission and guidance from a health care provider before participating in vigorous physical activity. The benefits and costs of such a suggestion are unknown. Does a recommendation for people to develop an activity plan with a health care provider prevent adverse events? Does it reduce participation in physical activity? If both, what is the balance at the population level? Are such recommendations justified for certain population subgroups? If so, which ones?

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Part G. Section 11: Understudied Populations

Introduction

The charge to the Physical Activity Guidelines Advisory Committee (PAGAC) was to review existing scientific literature to identify where sufficient evidence exists to develop comprehensive public health physical activity recommendations for all Americans and to target them as necessary for specific segments of the population. The higher levels of chronic disease risk and burden in racial/ethnic and/or lower socioeconomic status (SES) communities, and the growing cultural diversity of the United States, make these population segments a priority in considering such targeting. The primary focus of the PAGAC scientific review was research on primary prevention and health/fitness promotion, not research on the delivery of exercise as a therapy or treatment for specific disease conditions (e.g., physical therapy for musculoskeletal disease or injury, cardiac rehabilitation). However, the PAGAC recognized that many of the health benefits of physical activity for the general population also pertained to many people who have some health condition that typically excludes them from physical activity and health research. Included in these populations are people with various disabilities, women during pregnancy and the postpartum period, and races and ethnicities other than non-Hispanic whites. Therefore, the PAGAC decided to conduct a separate review of the scientific literature focusing on these three populations.

The first part of this chapter reviews the science published since 1995 evaluating the general health and fitness benefits of increased activity in persons with selected physical and cognitive disabilities. The second part provides a brief review of the science regarding physical activity performed by women during pregnancy and the postpartum period. The last section provides an overview of the science addressing the question, “Is there evidence that the physical activity dose for improving health and fitness should differ for people depending upon race or ethnicity?” Each PAGAC subcommittee was asked to consider this question in its review of the literature, but committee members agreed that it would help in better understanding this issue if the available evidence was summarized in this section of the report.

Review of the Science: Health Outcomes Associated With Physical Activity in People With Disabilities

Introduction

The lack of participation in beneficial physical activity is a serious public health concern for all Americans, but it is even more acute for people with disabilities, who are demonstrably at much greater risk of developing the types of serious health problems associated with a sedentary lifestyle. *Healthy People* 2010 outlines current levels of physical activity and exercise for various subpopulations in the United States based on cross-sectional surveys, as well as goals for the year 2010 (1). As shown in Table G11.1, individuals with disabilities are currently much less active than their non-disabled counterparts and participate in less regular and less vigorous physical activity. They also report substantially more secondary conditions that are directly or indirectly associated with their disability but are considered preventable (e.g., fatigue, weight gain, deconditioning, pain) (2).

Table G11.1. Healthy People 2010 (HP 2010) Goals for Increasing Physical Activity in Adults

	With Disabilities	Without Disabilities	HP 2010 Target
No leisure-time physical activity	56%	36%	20%
30 Minutes activity 5+ days per week	12%	16%	30%
20 Minutes vigorous physical activity for cardiorespiratory fitness 3+ days per week	13%	25%	30%

Patterns of low physical activity reported among people with disabilities raise serious concern about their health and well being, particularly as they enter their later years, when the effects of the natural aging process are compounded by years of sedentary living and severe deconditioning (3). Although substantial public health initiatives strive to prevent disease, injury, and *disability*, a growing recognition among public policy experts is the need to address people with disabilities as a target population who can benefit from health promotion activities, including increased participation in physical activity (4;5). Recognizing that people with disabilities are less physically active than the general population (6;7), have poorer health status (8), and in particular, are more likely to experience chronic and secondary conditions such as obesity, pain, fatigue, and depression (2), an examination of the existing evidence associated with the effects of physical activity in people with disabilities is urgently needed (9). A first step in this process is to (a) determine whether people with disabilities receive similar cardiovascular, musculoskeletal, metabolic, mental and functional health benefits as people without disabilities, and (b) understand if these benefits outweigh the risks of physical activity in these populations.

Overview of the Questions Asked

Eight categories of physical disability, 3 categories of cognitive disability, and 1 group of combined disabilities are the focus of this review (Table G11.2). These groups were selected because of the higher volume of research identified on these populations compared to other groups, such as spina bifida and polio, where very few research studies were identified.

Table G11.2. Categories of Disability

Physical Disabilities	Cognitive Disabilities	Combined Disabilities
1. Lower limb loss 2. Cerebral palsy 3. Multiple sclerosis 4. Muscular dystrophy 5. Parkinson's disease 6. Spinal cord injury 7. Stroke 8. Traumatic brain injury	1. Alzheimer's disease 2. Intellectual disability including Down syndrome 3. Mental illness	1. Two or more disability groups in same study

For these categories, the following questions were asked:

1. What is the evidence that physical activity improves cardiorespiratory fitness in people with disabilities?
2. What is the evidence that physical activity improves lipid profiles in people with disabilities?
3. What is the evidence that physical activity improves musculoskeletal health in people with disabilities?
4. What is the evidence that physical activity improves functional health in people with disabilities?
5. What is the evidence that physical activity reduces secondary conditions in people with disabilities?
6. What is the evidence that physical activity helps maintain healthy weight and improves metabolic health in people with disabilities?
7. What is the evidence that physical activity improves mental health in people with disabilities?

Following these discussions, the chapter addresses the safety concerns and complications associated with physical activity in people with physical and cognitive disabilities.

Data Sources and Process Used To Answer Questions

The *Physical Activity Guidelines for Americans* Scientific Database (see ***Part F: Scientific Literature Database Methodology*** for a detailed description of the Database and its development) included only a few manuscripts that evaluated the effects in populations with disabilities. Thus, a comprehensive literature review was conducted using the MEDLINE and CINAHL databases. Two abstractors combined several keywords associated with disability and physical activity or exercise. Reference lists in each individual article were also reviewed for additional articles, including meta-analytic articles and systematic review articles. The articles were included if they met the following inclusion criteria:

- Written in English;
- Publication date between January 1995 and November 2007;
- Subjects had one of the 11 disabilities listed in Table G11.2;
- Physical activity was the primary exposure variable;
- Covered the health outcomes listed in the preceding questions; and
- Peer-reviewed.

Studies were excluded if they: (1) involved therapeutic exercise modalities available primarily at a medical facility, such as body weight supported treadmill training or functional electrical stimulation, as the main exposure variable; (2) used single bouts of exercise; or (3) were conducted using qualitative methods or case study.

Each of the identified studies was classified into 3 types of study design: Randomized controlled trial (RCT), non-randomized trial with control group, and pre/post-test with no control group. RCT is listed as the highest level of evidence; non-randomized trials with a control group as middle level of evidence; and pre/post designs with no control group as the lowest level of evidence (10). No cross-sectional, retrospective observational, or prospective observational studies were included in the review.

Data Extraction

A total of 139 articles published between 1995 and 2007 and that met all inclusion criteria were identified and reviewed for this report. Data were independently extracted by 2 reviewers who have backgrounds in disability and rehabilitation using the following categories:

- **Participants/Subjects:** Number recruited; number analyzed; age; disability type; disability characteristics; number of years of disability before intervention.
- **Interventions:** Type of training (i.e., aerobic, strength, flexibility); exercise mode; training frequency; training duration; length of intervention; program progression; attendance and/or compliance; description of control condition.

- **Setting:** Supervised or unsupervised; home or community.
- **Outcome Measures:** Health outcomes associated with the intervention and divided into six categories: cardiorespiratory, musculoskeletal, metabolic including body weight, mental, functional, and secondary conditions.

Figure G11.1 illustrates the number and design type of reviewed trials by disability group. Trials investigating the effects of exercise on people with Stroke had the most number of intervention-related exercise articles (n=23), while lower limb loss had the lowest number of identified articles (n=2).

Types of Evidence

The type of available evidence used in this report to determine the effects of exercise on health outcomes in people with physical or cognitive disabilities was based on a modification of the criteria used by the US Agency for Healthcare Research and Quality (AHRQ, formerly known as the US Agency for Health Care Policy and Research) (11). We did not review the quality of each study (e.g., power, intent-to-treat, different testers on pre/post outcomes) as recommended by AHRQ and we also changed the categories of evidence to parallel the work of the Committee. Non-randomized trials were collapsed under the category of Pre/Post Studies with no Control Group (i.e., Non-RCT).

Level of Evidence

Type 1: Two or more RCTs with positive results and no studies reported significant negative effects.

Type 2a: One RCT with positive results and no studies reported significant negative effects.

Type 2b: At least one Non-RCT with positive results and no studies with significant negative effects.

Type 3a: Well designed prospective cohort studies and case-control studies.

Type 3b: Other observational studies – weak prospective cohort studies or case-control studies; cross-sectional studies or case series.

Type 4: Non-significant findings or no studies investigating the effects of exercise on people with disabilities.

Figure G11.1. Number of Articles Identified by Disability Group and Design (N=139)

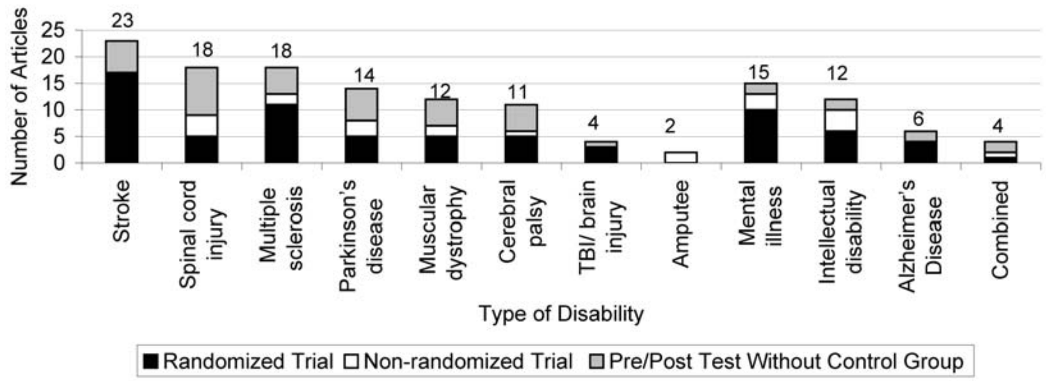

Figure G11.1. Data Points

Categories	Type of Disability	Randomized Trial	Non-Randomized Trial	Pre/Post Test Without Control Group
Neuromuscular	Stroke	17	0	6
Neuromuscular	Spinal cord injury	5	4	9
Neuromuscular	Multiple sclerosis	11	2	5
Neuromuscular	Parkinson's disease	5	3	6
Neuromuscular	Muscular dystrophy	5	2	5
Neuromuscular	Cerebral palsy	5	1	5
Neuromuscular	TBI/brain injury	3	0	1
Neuromuscular	Amputee	0	2	0
Cognitive	Mental illness	10	3	2
Cognitive	Intellectual disability	6	4	2
Cognitive	Alzheimer's Disease	4	0	2
Mixed	Combined	1	1	2
Total	**–**	72	22	45

Question 1. What Is the Evidence That Physical Activity Improves Cardiorespiratory Fitness in People With Disabilities?

Conclusions

Type 1 evidence indicates that cardiorespiratory fitness can be improved in people with Lower Limb Loss, Multiple Sclerosis, Spinal Cord Injury, Stroke, and Mental Illness. Type 2a evidence provides the same findings for people with Traumatic Brain Injury and Intellectual Disability, type 2b evidence provides these findings in persons with Cerebral Palsy, Muscular Dystrophy, and Alzheimer's Disease, and type 4 is indicative of no data or non-significant findings on Parkinson's Disease. Overall, the evidence is highly supportive of the use of physical activity in improving cardiorespiratory fitness among people with physical and cognitive disabilities.

Rationale

Twenty-one RCTs targeted improvements in cardiorespiratory fitness in persons with physical and cognitive disabilities (Table G11.3). Of these 21 RCTs, 18 (86%) reported significant favorable cardiorespiratory fitness outcomes. Of 25 non-RCTs, 21 (84%) reported significant favorable cardiorespiratory fitness outcomes.

Table G11.3. Physical Activity and Cardiorespiratory Fitness in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	2(12;13)	–	–	–	●	–	–	–
Physical: Cerebral Palsy	–	–	1(14)	–	–	–	●	–
Physical: Multiple Sclerosis	4(15-18)	1(19)	1(20)	1(21)	●	–	–	–
Physical: Muscular Dystrophy	–	–	4(22-25)	1(26)	–	–	●	–
Physical: Parkinson's Disease	–	–	–	–	–	–	–	●
Physical: Spinal Cord Injury	2(27;28)	–	7(29-35)	2(36;37)	●	–	–	–
Physical: Stroke	6(38-43)	–	1(44)	–	●	–	–	–
Physical: Traumatic Brain Injury	1(45)	–	1(46)	–	–	●	–	–

Table G11.3. Physical Activity and Cardiorespiratory Fitness in People With Disabilities (continued)

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Cognitive: Alzheimer's Disease	–	–	2(47;48)	–	–	–	●	–
Cognitive: Intellectual Disability	1(49)	1(50)	2(51;52)	–	–	●	–	–
Cognitive: Mental Illness[c]	2(53;54)	1(55)	–	–	●	–	–	–
Combined	–	–	2(56;57)	–	–	–	•	–

[a] S, Significant findings; [b] NS, Non-significant findings; [c] Major depression disorder

Question 2. What Is the Evidence That Physical Activity Improves Lipid Profiles in People With Disabilities?

Conclusions

The evidence on the use of physical activity for cardiovascular risk reduction is less clear than it is for cardiorespiratory fitness. Two RCTs and 2 non-RCTs reported significant reductions in total cholesterol and triglycerides, and two non-RCTs found no differences in cholesterol reduction after the exercise intervention.

Rationale

Health outcomes targeted in these studies included triglycerides and total cholesterol. Among persons with physical disabilities, 3 (75%) of 4 studies showed reduction in cholesterol (spinal cord injury) and triglycerides (multiple sclerosis) (Table G11.4). Among persons with cognitive disability, 1 (50%) of 2 studies reported reduction in triglycerides (mental illness). In 3 of the 4 studies, subjects had high cholesterol and triglycerides at baseline.

Table G11.4. Physical Activity and Lipid Profiles in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	–	–	–	–	–	–	●
Physical: Multiple Sclerosis[c]	1(17)	–	1(58)	–	–	●	–	–
Physical: Muscular Dystrophy	–	–	–	–	–	–	–	●
Physical: Parkinson's Disease	–	–	–	–	–	–	–	●
Physical: Spinal Cord Injury[d]	–	–	1(33)	1(30)	–	–	●	–
Physical: Stroke	–	–	–	–	–	–	–	●
Physical: Traumatic Brain Injury	–	–	–	–	–	–	–	●
Cognitive: Alzheimer's Disease	–	–	–	–	–	–	–	●
Cognitive: Intellectual Disability[d]	–	–	–	1(59)	–	–	–	●
Cognitive: Mental Illness[c]	1(60)	–	–	–	–	●	–	–
Combined	–	–	–	–	–	–	–	●

[a] S, Significant findings; [b] NS, Non-significant findings; [c] Triglycerides; [d] Total cholesterol

Question 3. What Is the Evidence That Physical Activity Improves Musculoskeletal Health in People With Disabilities?

Conclusions

Type 1 evidence indicates that resistance exercise, aerobic exercise, or a combination of resistance and aerobic exercise all increase muscle strength in various subgroups with physical and cognitive disabilities. Although less evidence exists on flexibility interventions for the 11 population subgroups, in the 4 RCTs conducted on individuals with Parkinson's disease (n=1), Stroke (n=2) and Traumatic Brain Injury (n=1), findings were significant for each disability group. Of the 4 non-RCTs on flexibility training, 2 studies, which involved subjects with Spinal Cord Injury and Combined Disabilities (i.e., physical and intellectual disabilities), were found to be significant. The other two non-RCTs were not significant in persons with Multiple Sclerosis and Intellectual Disability. Type 1 evidence finds that flexibility can be improved in persons with Stroke, and type 2a evidence finds that it can be improved in persons with Parkinson's disease and Traumatic Brain Injury.

Type 2a evidence exists on the use of exercise in improving bone mineral density (BMD) in people with physical and cognitive disabilities. Only 2 studies were identified that used an exercise exposure to improve BMD, one in youth with Cerebral Palsy and the other study on adults with unilateral Stroke. Both studies supported the use of exercise in improving BMD in these populations, but more evidence is needed to determine whether these findings will be supported by further studies.

Rationale

Muscle Strength

Table G11.5 summarizes the 37 exercise interventions addressing improvements in muscle strength. Of the 17 RCTs, 14 (82%) studies reported significant positive effects. Of the 20 non-RCTs, 19 (95%) trials reported significant improvements in muscle strength.

Flexibility

Table G11.6 summarizes the intervention research on flexibility. Four RCTs targeted improvements in flexibility in persons with physical disabilities. All 4 (100%) studies reported significant positive findings. Of the 4 non-RCTs, 2 (50%) reported significant improvements in flexibility.

Bone Mineral Density

Two studies found in the literature used exercise to improve BMD in people with disabilities. In the first study (RCT), children with cerebral palsy were exposed to a program of various types of upper and lower extremity exercises. The program consisted of 1 hour-long session per week for 8 weeks, which was increased to 3 sessions per week for the next 24 weeks. The program showed significant improvement in BMD compared to controls (61). In the second RCT, researchers concluded that exercise can slow the decline in bone loss in the affected femoral neck of people with unilateral Stroke (41).

Table G11.5. Physical Activity and Muscle Strength in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	1(62)	1(63)	5(64-68)	–	–	●	–	–
Physical: Multiple Sclerosis	2(17;69)	-	1(70)	–	●	–	–	–
Physical: Muscular Dystrophy[c]	1(71)	1(72)	1(73)	–	–	●	–	–
Physical: Parkinson's Disease	1(74)	–	1(75)	–	–	●	–	–
Physical: Spinal Cord Injury	1(76)	–	5 (20;34;36;40;77)	–	–	●	–	–
Physical: Stroke	5 (38;41;43;78;79)	–	3(80-82)	–	●	–	–	–
Physical: Traumatic Brain Injury	–	1(83)	–	–	–	–	–	●
Cognitive: Alzheimer's Disease	–	–	1(47)	–	–	–	●	–
Cognitive: Intellectual Disability	3(49;84;85)	–	–	1(86)	●	–	–	–
Cognitive: Mental Illness	–	–	–	–	–	–	–	●
Combined	–	–	2(57;87)	–	–	–	●	–

[a]S, Significant findings; [b]NS, Non-significant findings; [c]NS in Myotonic Dystrophy group, S in Charcot-Marie-Tooth group; reference was counted only one time.

Table G11.6. Physical Activity and Flexibility in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	–	–	–	–	–	–	●
Physical: Multiple Sclerosis	–	–	–	1(88)	–	–	–	●
Physical: Muscular Dystrophy	–	–	–	–	–	–	–	●
Physical: Parkinson's Disease	1(89)	–	–	–	–	●	–	–
Physical: Spinal Cord Injury	–	–	1(37)	–	–	–	●	–
Physical: Stroke	2(43;90)	–	–	–	●	–	–	–
Physical: Traumatic Brain Injury	1(45)	–	–	–	–	●		
Cognitive: Alzheimer's Disease	–	–	–	–	–	–	–	●
Cognitive: Intellectual Disability	–	–	–	1(86)	–	–	–	●
Cognitive: Mental Illness	–	–	–	–	–	–	–	●
Combined	–	–	1(57)	–	–	–	●	–

[a] S, Significant findings; [b] NS, Non-significant findings

Question 4. What Is the Evidence That Physical Activity Improves Functional Health in People With Disabilities?

Conclusions

Functional health has a broad association with several performance measures associated with basic and instrumental activities of daily living (ADL and IADL). This includes walking speed, walking distance, quality of life, functional independence, and balance. Evidence from a variety of studies supports the use of exercise to improve walking speed and distance and other measures of functional health across a range of disabilities.

A total of 74 interventions targeted one or more measures of functional health under the categories of walking speed, walking distance, quality of life/well-being, functional independence, and balance. These studies provided type 1 evidence (Table G11.7) for the use of exercise in improving walking speed in persons with Multiple Sclerosis, Stroke, and Intellectual Disability, type 2a evidence for the use of exercise in persons with Parkinson's disease and Alzheimer's disease, and type 2b evidence for the use of exercise in persons with Cerebral Palsy and Spinal Cord Injury (where the propulsion speed of pushing a wheelchair is used as an equivalent to walking speed). The studies provided type 1 evidence that walking distance can be improved in persons with Multiple Sclerosis, Stroke, and Intellectual Disability (Table G11.8) and type 2a evidence that walking speed can be improved in people with Parkinson's disease. On Quality of Life (Table G11.9), the studies provided type 1 evidence to support exercise for people with Multiple Sclerosis, Spinal Cord Injury, and Stroke and type 2a evidence to support exercise in people with Muscular Dystrophy, Alzheimer's disease, Intellectual Disability, and Mental Illness. For Functional Independence (Table G11.10), the studies provided type 1 evidence supporting the use of exercise in people with Stroke and type 2a evidence supporting exercise in people with Multiple Sclerosis, Parkinson's disease, Traumatic Brain Injury, and Alzheimer's disease. For Balance (Table G11.11), the studies provided type 1 evidence supporting the use of exercise in improving balance only in people with Parkinson's disease and Stroke. The studies had type 2b or 4 evidence for the other disability subgroups.

Rationale

Walking Speed

Table G11.7 summarizes the 35 intervention studies that used walking speed as a health outcome. Of the 19 RCTs, 13 (68%) reported significant increases in walking speed. Of the 16 Non-RCTs, 10 (63%) reported significant increases in walking speed.

Table G11.7. Physical Activity and Walking Speed in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	1(91)	2(64;66)	2(65;67)	–	–	●	–
Physical: Multiple Sclerosis	3 (18;92;93)	1(69)	1(94)	3 (70;88;95)	●	–	–	–
Physical: Muscular Dystrophy	–	–	–	–	–	–	–	●

Table G11.7. Physical Activity and Walking Speed in People With Disabilities (continued)

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Parkinson's Disease	1(96)	–	2(97;98)	–	–	●	–	–
Physical: Spinal Cord Injury[c]	–	–	1(77)	–	–	–	●	–
Physical: Stroke	6 (38;39;79;99-101)	3 (78;102;103)	3 (80;104;105)	1(82)	●	–	–	–
Physical: Traumatic Brain Injury	–	–	–	–	–	–	–	●
Cognitive: Alzheimer's Disease	1(106)	–	–	–	–	●	–	–
Cognitive: Intellectual Disability	2(107;108)	–	1(109)	–	●	–	–	–
Cognitive: Mental Illness	–	–	–	–	–	–	–	●
Combined	–	1(110)	–	–	–	–	–	●

[a] S, Significant findings; [b] NS, Non-significant findings; [c] Specific to propulsion speed pushing a wheelchair

Walking Distance

Table G11.8 summarizes the 18 interventions that used walking distance as an outcome. Of the 13 RCTs, 10 (77%) reported significant increases in walking distance. Of the five Non-RCTs, four (80%) reported significant increases in walking distance.

Table G11.8. Physical Activity and Walking Distance in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	–	–	–	–	–	–	●
Physical: Multiple Sclerosis	2 (18;111)	–	1(94)	–	●	–	–	–

Table G11.8. Physical Activity and Walking Distance in People With Disabilities (continued)

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Muscular Dystrophy	–	–	-	–	–	–	–	●
Physical: Parkinson's Disease	1(96)	–	1(112)	–	–	●	–	–
Physical: Spinal Cord Injury	–	–	–	–	–	–	–	●
Physical: Stroke	4 (39;41;99;100)	1(101)	1(104)	1(105)	●	–	–	–
Physical: Traumatic Brain Injury	–	–	–	–	–	–	–	●
Cognitive: Alzheimer's Disease	–	1(113)	1(47)	–	–	–	●	–
Cognitive: Intellectual Disability[c]	3 (50;107;108)	–	–	–	●	–	–	–
Cognitive: Mental Illness[d]	–	1(114)	–	–	–	–	–	●
Combined	–	–	–	–	–	–	–	●

[a] S, Significant findings; [b] NS, Non-significant findings; [c] Down syndrome; [d] Schizophrenia

Quality of Life and Well-Being

Table G11.9 summarizes the 27 interventions on quality of life/well-being. Of the 19 RCTs, 13 studies (68%) reported significant positive findings. Seven (88%) of the eight non-RCTs (n=8) demonstrated significant improvements in quality of life or well-being.

Table G11.9. Physical Activity and Quality of Life in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	–	–	–	–	–	–	●

Table G11.9. Physical Activity and Quality of Life in People With Disabilities (continued)

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Multiple Sclerosis[c]	3 (18;19;115)	3 (15;18;84)	1(21)	1(88)	●	–	–	–
Physical: Muscular Dystrophy	1(116)	1(117)	1(25)	–	–	●	–	–
Physical: Parkinson's Disease	–	1(118)	3 (98;119;120)	–	–	–	●	–
Physical: Spinal Cord Injury	2(76;121)	–	–	–	●	–	–	–
Physical: Stroke[d]	4 (79;90;103;122)	1(90)	–	–	●	–	–	–
Physical: Traumatic Brain Injury	–	–	–	–	–	–	–	●
Cognitive: Alzheimer's Disease	1(123)	–	–	–	–	●	–	–
Cognitive: Intellectual Disability	1(124)	–	1(109)	–	–	●	–	–
Cognitive: Mental Illness	1(125)	–	1(126)	–	–	●	–	–
Combined	–	–	–	–	–	–	–	●

[a] S, Significant findings; [b] NS, Non-significant findings; [c]One RCT(18) showed a significant finding in well-being (measured by the emotional well-being subscore in the Multiple Sclerosis Quality of Life-54 scale) but a non-significant finding in quality of life (measured by the overall score in the Multiple Sclerosis Quality of Life-54); [d]One RCT(90) reported a significant finding in well-being measured by the Profile of Mood States instrument) but a non-significant finding in quality of life (measured by the Stroke Specific Quality of Life Scale).

Functional Independence

Table G11.10 summarizes the 35 interventions on functional independence, which was primarily measured by an assessment of ADL, and IADL or motor function (i.e., motor control, function of upper/lower extremity, motor skills). A total of 17 RCTs targeted improvements in functional independence primarily in people with physical disabilities (14 of the 17 RCTs). Out of these 17 RCTs, 9 (53%) reported significant outcomes. In addition, 18 non-RCTs targeted people with physical disabilities, and 14 (82%) of these studies reported significant findings on functional independence.

Table G11.10. Physical Activity and Functional Independence in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	1(62)	5(14;64-66;68)	1(67)	–	–	●	–
Physical: Multiple Sclerosis	1(17)	–	–	–	–	●	–	–
Physical: Muscular Dystrophy	–	–	–	–	–	–	–	●
Physical: Parkinson's Disease[c]	1(127)	1(89)	5 (98;120;128-130)	1(129)	–	●	–	–
Physical: Spinal Cord Injury	–	–	2(36;77)	–	–	–	●	–
Physical: Stroke[d]	5 (78;100;101;103;131)	4 (78;99;101;102)	2(104;105)	2(80;82)	●	–	–	–
Physical: Traumatic Brain Injury	1(83)	–	–	–	–	●	–	–
Cognitive: Intellectual Disability	–	–	–	–	–	–	–	●
Cognitive: Mental Illness	–	–	–	–	–	–	–	●
Combined	–	1(110)	–	–	–	–	–	●

[a] S, Significant findings, [b] NS, Non-significant findings, [c] one Non-RCT (129) showed a significant finding in motor function but a non-significant finding in functional independence; [d] two RCTs (78;101) reported a significant finding in motor function in the lower extremity but a non-significant finding on functional independence.

Balance

Table G11.11 summarizes the 21exercise interventions on balance. Of the 13 RCTs, 6 (46%) reported significant findings. Of the 8 non-RCTs, 6 (75%) reported significant positive findings. The majority of studies were conducted on Parkinson's disease and Stroke.

Table G11.11. Physical Activity and Balance in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	–	1(64)	–	–	–	●	–
Physical: Multiple Sclerosis	–	1(69)	–	–	–	–	–	●
Physical: Muscular Dystrophy	–	1(116)	–	–	–	–	–	●
Physical: Parkinson's Disease[c]	4 (74;89;96;118)	1(118)	1(98)	1(129)	●	–	–	–
Physical: Spinal Cord Injury	–	–	–	1(132)	–	–	–	●
Physical: Stroke	2 (39;133)	3 (38;41;101)	3 (82;104;105)	–	●	–	–	–
Physical: Traumatic Brain Injury	–	–	–	–	–	–	–	●
Cognitive: Alzheimer's Disease	–	–	–	–	–	–	–	●
Cognitive: Intellectual Disability	–	–	1(109)	–	–	–	●	–
Cognitive: Mental Illness	–	–	–	–	–	–	–	●
Combined	–	1(110)	–	–	–	–	–	●

[a] S, Significant findings; [b] NS, Non-significant findings; [c] One RCT (118) under Parkinson's disease indicated a lower prevalence of falls among the exercise group compared to the control group but also reported a non-significant finding on the Berg Balance Score.

Question 5. What Is the Evidence that Physical Activity Reduces Secondary Conditions in People With Disabilities?

Conclusions

Type 1 evidence exists for the use of exercise in reducing fatigue in people with Multiple Sclerosis, type 2a evidence supports exercise in persons with Muscular Dystrophy, and type 4 evidence supports exercise in the remaining subgroups. In addition, type 1 evidence indicates that pain can be reduced in people with Spinal Cord Injury, type 2a evidence based on one study has similar findings for people with Down syndrome, and type 4 evidence exists that exercise can reduce pain on the other subgroups.

Introduction

Individuals with disabilities are likely to be at increased risk for a number of preventable health problems referred to as *secondary conditions*. According to Chapter 6 of the *Healthy People 2010* report (1), secondary conditions are defined as "...physical, medical, cognitive, emotional, or psychosocial consequences to which persons with disabilities are more susceptible by virtue of an underlying impairment, including adverse outcomes in health, wellness, participation and quality of life (p. 163)." Several secondary conditions are prominent among people with disabilities, and pain and fatigue are reported to be two of the most common secondary conditions observed in people with physical and cognitive disabilities (9).

Rationale

Fatigue

Table G11.12 summarizes the 10 interventions on fatigue. Of the 8 RCTs, 4 (50%) reported significant positive health outcomes. Of the 2 non-RCTs, both (100%) showed significant positive reductions in fatigue. The major target subgroup was persons with Multiple Sclerosis.

Table G11.12. Physical Activity and Fatigue Reduction in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	–	–	–	–	–	–	●
Physical: Multiple Sclerosis	3 (17;115;134)	3 (18;19;135)	2 (21;70)	–	●	–	–	–
Physical: Muscular Dystrophy	1(117)	–	–	–	–	●	–	–
Physical: Parkinson's Disease	–	–	–	–	–	–	–	●
Physical: Spinal Cord Injury	–	–	–	–	–	–	–	●

Table G11.12. Physical Activity and Fatigue Reduction in People With Disabilities (continued)

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Stroke	–-	–	–	–	–	–	–	●
Physical: Traumatic Brain Injury	–	–	–	–	–	–	–	●
Cognitive: Alzheimer's Disease	–	–	–-	–	–	–	–	●
Cognitive: Intellectual Disability	–	–	–	–	–	–	–	●
Cognitive: Mental Illness	–	–	–	–	–	–	–	●
Combined	–	1(136)	–	–	–	–	–	●

[a] S, Significant findings; [b] NS, Non-significant findings

Pain

Table G11.13 summarizes the evidence on 5 exercise interventions targeting musculoskeletal pain. Two RCTs and 2 non-RCTs indicated significant reductions in pain in people with Spinal Cord Injury. Three studies targeted reduction in shoulder pain in persons with Spinal Cord Injury, and the other study evaluated general pain. Only one RCT involving individuals with cognitive disabilities was identified, and this study reported significant reductions in pain associated with intermittent claudication in persons with Down syndrome.

Table G11.13. Physical Activity and Pain Reduction in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	–
Physical: Cerebral Palsy	–	–	–	–	–	–	–	–
Physical: Multiple Sclerosis	–	–	–	–	–	–	–	–
Physical: Muscular Dystrophy	–	–	–	–	–	–	–	–

Table G11.13. Physical Activity and Pain Reduction in People With Disabilities (continued)

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Parkinson's Disease	–	–	–	–	–	–	–	–
Physical: Spinal Cord Injury	2 (76;121)	–	2 (34;137)	–	●	–	–	–
Physical: Stroke	–	–	–	–	–	–	–	–
Physical: Traumatic Brain Injury	–	–	–	–	–	–	–	–
Cognitive: Alzheimer's Disease	–	–	–	–	–	–	–	–
Cognitive: Intellectual Disability[c]	1(108)	–	–	–	–	●	–	–
Cognitive: Mental Illness	–	–	–	–	–	–	–	–
Combined	–	–	–	–	–	–	–	–

[a] S, Significant findings; [b] NS, Non-significant findings; [c]People with Down syndrome who suffered from intermittent claudication

Question 6. What Is the Evidence That Physical Activity Helps Maintain Healthy Weight and Improve Metabolic Health?

Conclusions

Type 2a evidence indicates that exercise can improve body composition in persons with Stroke, Intellectual Disability, Mental Illness, Traumatic Brain Injury, and a combined group of individuals with different types of physical disabilities. Type 4 evidence suggests the same finding for the remaining disability subgroups. On metabolic factors, type 2a evidence exists for improvements in fasting glucose and insulin sensitivity in two disability subgroups (Stroke and Mental Illness) and type 4 evidence shows the same result for the remaining subgroups.

Rationale

Body Composition

Table G11.14 summarizes the 19 interventions on body composition including those focused on body weight, body fat, body mass index (BMI), and waist circumference. Of the 10 RCTs, 5 studies (50%) reported significant positive effects in decreasing body weight. Of the 9 non-RCTs, 2 (22%) reported significant positive findings on body composition.

Table G11.14. Physical Activity and Body Composition in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	–	–	–	–	–	–	●
Physical: Multiple Sclerosis	–	1(17)	–	1(58)	–	–	–	●
Physical: Muscular Dystrophy	–	–	–	1(138)	–	–	–	●
Physical: Parkinson's Disease	–	–	–	–	–	–	–	●
Physical: Spinal Cord Injury	–	–	–	3 (33;77;139)	–	–	–	●
Physical: Stroke	1(43)	1(40)	–	–	–	●	–	–
Physical: Traumatic Brain Injury	1(45)	–	–	1(46)	–	●	–	–
Cognitive: Alzheimer's Disease	–	–	–	–	–	–	–	●
Cognitive: Intellectual Disability[c]	1(49)	1(50)	–	–	–	●	–	–
Cognitive: Mental Illness[d]	1(60)	2(114)	2(140;141)	1(136)	–	●	–	–
Combined	1(110)	–	–	–	–	●	–	–

[a] S, Significant findings; [b] NS, Non-significant findings; [c] Down syndrome; [d] Schizophrenia

Metabolic Health

Three RCTs also targeted improvements in metabolic factors (fasting glucose, insulin sensitivity, fasting insulin, and insulin-like growth factor-binding protein-3). Two (67%) of these 3 studies reported significant positive findings in people with Stroke (40) and Schizophrenia (60) while one study (33%) reported non-significant findings in people with Spinal Cord Injury (27).

Question 7. What Is the Evidence That Physical Activity Improves Mental Health in People With Disabilities?

Conclusions

Type 1 evidence indicates that exercise can reduce depression in people with Alzheimer's disease and Mental Illness. Type 2a evidence shows the same result in persons with Multiple Sclerosis, Spinal Cord Injury, Stroke, and Intellectual Disability, as does type 4 evidence in the remaining subgroups. The highest level of evidence was reported in people with Mental Illness (6 RCTs reporting significant outcomes). Physical activity also appears to have beneficial effects on several other mental health outcomes including self-esteem, quality of sleep, interpersonal relationships, disruptive behavior, negative symptoms, and anxiety. No type 1 studies were identified for any of these outcomes. However, type 2a evidence was reported for beneficial effects of self-esteem (Muscular Dystrophy, Traumatic Brain Injury, and Intellectual Disability), quality of sleep (Spinal Cord Injury and Alzheimer's disease), interpersonal relationships (Stroke and Mental Illness), and negative symptoms (Mental Illness).

Rationale

Depression

Table G11.15 summarizes the 20 interventions targeting reduction in depression. Out of the 17 RCTs, 12 studies (71%) reported significant reductions in depression. Three non-RCTs (100%) also reported significant reductions in depression.

Table G11.15. Physical Activity and Depression in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	●
Physical: Cerebral Palsy	–	–	–	–	–	–	–	●
Physical: Multiple Sclerosis	1(17)	–	1(21)	–	–	●	–	
Physical: Muscular Dystrophy	–	–	–	–	–	–	–	●
Physical: Parkinson's Disease	–	–	–	–	–	–	–	●
Physical: Spinal Cord Injury	1(121)	1(76)	–	–	–	●	–	–

Table G11.15. Physical Activity and Depression in People With Disabilities (continued)

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Stroke	1(122)	–	–	–	–	●	–	–
Physical: Traumatic Brain Injury	–	–	–	–	–	–	–	●
Cognitive: Alzheimer's Disease	2 (123;142)	1(106)	–	–	●	–	–	–
Cognitive: Intellectual Disability	1(124)	–	–	–	–	●	–	–
Cognitive: Mental Illness	6 (54;55;143-146)	2 (53;125)	1(126)	–	●	–	–	–
Combined	–	1(110)	1(56)	–	–	–	●	

[a] S, Significant findings; [b] NS, Non-significant findings

Other Major Mental Health Outcomes

Table G11.16 summarizes the evidence on 12 exercise interventions targeting other mental health outcomes in persons with disabilities, including self-esteem, quality of sleep, interpersonal relationships, negative psychiatric symptoms, anxiety, and disruptive behavior. In people with Muscular Dystrophy, Traumatic Brain Injury, and Intellectual Disability, the improved health outcome was self-esteem. In people with Spinal Cord Injury and Alzheimer's disease, quality of sleep improved; people with Mental Illness had reduced negative psychiatric symptoms and increased interpersonal relationships; and people with Stroke reported improvements in interpersonal relationships.

Table G11.16. Physical Activity and Other Major Mental Health Outcomes in People With Disabilities

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Lower Limb Loss	–	–	–	–	–	–	–	–
Physical: Cerebral Palsy	–	–	–	–	–	–	–	–

Table G11.16. Physical Activity and Other Major Mental Health Outcomes in People With Disabilities (continued)

Disabilities	Number of Studies [reference] RCT S[a]	Number of Studies [reference] RCT NS[b]	Number of Studies [reference] Non-RCT S	Number of Studies [reference] Non-RCT NS	Type of Evidence 1	Type of Evidence 2a	Type of Evidence 2b	Type of Evidence 4
Physical: Multiple Sclerosis	–	–	–	–	–	–	–	–
Physical: Muscular Dystrophy[c]	1(116)	–	1(24)	–	–	●	–	–
Physical: Parkinson's Disease	–	–	–	–	–	–	–	–
Physical: Spinal Cord Injury[d]	1(147)	–	–	–	–	●	–	–
Physical: Stroke[e]	1(90)	–	–	–	–	●	–	–
Physical: Traumatic Brain Injury[c]	1(83)	–	–	–	–	●	–	–
Cognitive: Alzheimer's Disease[d]	1(142)	–	–	–	–	●	–	–
Cognitive: Alzheimer's Disease[f]	–	1(106)	–	–	–	–	–	●
Cognitive: Intellectual Disability[c]	1(124)	–	–	–	–	●	–	–
Cognitive: Mental Illness[g]	1(145)	–	–	–	–	●	–	–
Cognitive: Mental Illness[e]	1(145)	–	1(148)	–	–	●	–	–
Combined[h]	–	1(110)	–	–	–	–	–	●

[a] S, Significant findings; [b] NS, Non-significant findings; [c] self-esteem; [d] quality of sleep; [e] interpersonal relationships; [f] disruptive behavior; [g] negative symptoms; [h] anxiety

Exercise Doses in the Studies

The majority of studies reviewed in this report included doses of exercise that are typically used in studies targeting the general population. Intensity of cardiorespiratory exercise was set at 50% or higher of target heart rate reserve or VO_{2peak}. Frequency of exercise ranged from 3 to 5 days a week and duration lasted from 30 to 60 minutes per session. The precise quantitative characteristics of the dose-response relationship between improvements in various health outcomes, however, still requires additional research before certain conclusions can be made regarding what doses effect what outcomes in targeted disability groups.

Question 8. What Do We Know About the Safety of Exercise in People With Disabilities?

Introduction

Among some health care professionals, an underlying perception exists that exercise *may* present an increased risk of injury for certain individuals with disabilities. This section provides an overview of the available literature describing issues associated with safety of exercise in people with physical and cognitive disabilities from the 139 articles that the Understudied Populations subcommittee reviewed for this chapter. The 139 exercise trials included 2,961 subjects exposed to an exercise intervention and 1,832 control subjects. The duration of the trials ranged from 1 week to 52 weeks.

Two abstractors carefully reviewed the Methods, Results, and Discussion sections of each article to identify reported side effects or adverse events. In particular, the abstractors focused on the reasons, when available, that the subject withdrew from the study, to determine whether it was related to the exercise exposure. The data are reported in frequencies and percentages and separated by exercise and control groups. The information contained in this section includes the most commonly reported complications or adverse events reported for each disability subgroup.

To determine whether a reported event was considered a complication (not serious) or adverse event (serious), we considered the following criteria from the Office for Human Research Protections (OHRP, 2007) (149): event was (1) undesirable in nature; (2) related or possibly related to the intervention; and (3) harmful to the participant either physically or psychologically. For the purpose of this review, the subcommittee modified these criteria to classify health complications associated with the intervention as *not serious adverse events* and *serious adverse events*. Serious adverse events frequently caused participants to drop out of the study.

What Is the Frequency of Reported Adverse Events Among People With Disabilities in the Exercise and Control Groups?

Adverse events were reported for 53 exercise subjects and 11 control subjects (Table G11.17). The percentage of exercise subjects (1.8%) and control subjects (0.6%) with any reported adverse event was not substantially different. Similarly, the percentage of exercise subjects (1.1%) and control subjects (0.6%) reported to have an adverse event serious enough to cause them to drop out of the study also were not substantially different.

Table G11.17. Number and Percentage of Subjects With Adverse Events by Seriousness of Event and Exposure Group

Exposure Group	Serious[a]	Non-serious	Total
Exercise Groups (n=2961)	34 (1.1%)	19 (0.6%)	53 (1.8%)
Control Groups (n=1832)	11 (0.6%)	0 (0.0%)	11 (0.6%)

[a] Serious adverse events involved those in which the subject dropped out of the study.

What Were the Commonly Reported Adverse Events in Exercise Trials Among People With Disabilities?

This review of evidence identified very few reported adverse events associated with exercise in people with physical and cognitive disabilities. Disability-related risks and activity-related risks are two common issues related to exercise training interventions in people with disabilities (150). We reviewed all the reported serious and non-serious adverse events and arranged them into 4 categories: (a) progression or recurrence of disease (i.e., disability-dependent risks) including recurrent Stroke or Multiple Sclerosis exacerbation, and/or worsening of conditions associated with the disability such as elevated spasticity, bladder spasms, mild seizure, recurrence of inguinal hernia, and increased depression; (b) cardiovascular problems including angina symptoms, dizziness, drop in blood pressure, acute myocardial infarction, and abnormal electrocardiogram; (c) falls; and (d) exercise-related musculoskeletal problems, including muscle soreness, pain, and increased fatigue.

Among the total number of adverse events [serious + non-serious] reported in the exercise group (n=53) (Table G11.18), musculoskeletal problems were the most commonly reported adverse event (n=24, 45%). Falls, cardiovascular problems, and increased fatigue were the other adverse events reported but occurred at a much lower rate. Table G11.18 also illustrates that recurrent Stroke, exacerbation in persons with Multiple Sclerosis, and cardiovascular problems were the major reported adverse events in the control group. A detailed overview of complications for each specific disability group can be found in Table G11.A1 (this table can be accessed at http://www.health.gov/paguidelines/report/).

Table G11.18. Classification, Number, and Percentage of Serious/Non-Serious Adverse Events in Exercise and Control Groups

Classification of Adverse Events	Exercise Group Percent (n/N)	Control Group Percent (n/N)
Progression or Recurrence of Disease: Recurrent stroke[a]	1.1% (6/538)	0.6% (2/335)
Progression or Recurrence of Disease: Mild seizure[a]	0.2 % (1/538)	0.0% (0/335)
Progression or Recurrence of Disease: Recurrence of inguinal hernia[a]	0.2 % (1/538)	0.0% (0/335)

Table G11.18. Classification, Number, and Percentage of Serious/Non-Serious Adverse Events in Exercise and Control Groups (continued)

Classification of Adverse Events	Exercise Group Percent (n/N)	Control Group Percent (n/N)
Progression or Recurrence of Disease: Exacerbations of multiple sclerosis[b]	1.1% (4/363)	1.9% (5/266)
Progression or Recurrence of Disease: Increased spasticity[b]	0.6% (2/363)	0.0% (0/266)
Progression or Recurrence of Disease: Increased depression[c]	0.2% (1/522)	0.0% (0/210)
Progression or Recurrence of Disease: Bladder spasms[d]	0.5 (1/208)	0.0% (0/75)
Falls	0.2% (5/2961)	0.0% (0/1832)
Cardiovascular Problems	0.1% (4/2961)	0.1% (2/1832)
Musculoskeletal Problem: Soreness or pain	0.8% (24/2961)	0.05% (1/1832)
Musculoskeletal Problem: Fatigue	0.1% (4/2961)	0.05% (1/1832)

[a]Includes only subjects in studies of persons with a history of stroke; [b]Includes only subjects in studies of persons with multiple sclerosis; [c]Includes only subjects in studies of persons with mental illness; [d]Includes only subjects in studies of persons with spinal cord injury.

What Adverse Events or Complications Are Concerns for Individuals With Stroke Who Want To Participate in a Physical Activity Program?

People with Stroke can exercise safely without serious adverse events by performing a careful prescreening exam and being supervised during exercise. No data indicate that exercise will increase the rate of recurrent Stroke if the appropriate monitoring and precautions are taken.

Among the 23 reviewed trials in which 538 Stroke survivors participated in some type of exercise intervention, 6 participants (1.1%) experienced a recurrent Stroke (39;103). In controls (n=335), recurrent Stroke occurred in 2 participants (0.6%) (102). The incidence of recurrent Stroke in the exercise group was lower than the incidence rate (2.9% to 6.0%) reported among individuals 3 to 6 months after their Stroke who are not involved in an exercise intervention (101).

Angina symptoms, dizziness, mild seizure, and drop in blood pressure during exercise or VO_{2peak} testing were reported in 2 studies (43;78). All reported side effects improved and all participants, with the exception of one individual who had a drop in post-exercise blood pressure and was removed from the study, received medical clearance to complete the exercise trial. Complications occurred in 2 Stroke participants who reported excess fatigue and dropped out of the study (41;131). Three other participants experienced back or knee pain but were able to complete the intervention (82).

Does Exercise Increase the Incidence of Exacerbation in Individuals With Multiple Sclerosis?

Although it is important to closely monitor any changes in disease symptoms for people with Multiple Sclerosis during and after the exercise training sessions, the concern of potential worsening symptoms related to the exercise exposure does not appear to be justified based on this literature review. This finding is in agreement with a recent report by Ginis and Hicks (7), who were charged with the development of a physical activity guide for Canadians with physical disabilities. In particular, there is no scientific evidence to support the notion that individuals with certain forms of Multiple Sclerosis may have worsening symptoms related to increased core temperature during/after exercise (7).

A total of 16 exercise trials involving persons with Multiple Sclerosis were reviewed. Among the participants in the exercise groups (n=363), 4 experienced musculoskeletal problems (1.1%), 2 reported elevated spasticity (0.6%), and 4 had an exacerbation (1.1%). In terms of the total number of subjects in the control groups (n=266), 1 subject experienced knee pain (0.4%) and 5 subjects had an exacerbation (1.9%). More specifically, 3 RCTs indicated no difference in relapse symptoms between the exercise and control groups (15;18;19). One trial reported that 2 participants in the exercise group experienced exacerbations while none did in the control group (115). However, 2 other trials reported that only participants in the control group (n=3) had an exacerbation of symptoms compared to no relapse in the exercise groups (16;69). Two studies indicated adverse events related to the exercise exposure. Two subjects in the intervention group experienced elevated spasticity of the lower extremity after completing the exercise test (16), and a few participants reported temporary low back muscle soreness (n=1) and leg muscle soreness (n=3) during the initial training period (70). Based on this literature review, there is currently no evidence to support the notion that exercise imposes a higher risk of exacerbation or harm in people with Multiple Sclerosis. This finding is consistent with a recent report published in Canada (7) that concluded that exercise has no effect on disease progression and should be an important component of disease management.

Is It Safe for People With Muscular Dystrophy to Exercise?

Back pain, muscle soreness, and feelings of fatigue were the most commonly reported adverse events associated with exercise in subjects with Muscular Dystrophy. Among 230 subjects in the exercise groups of 12 examined studies, 7 participants reported musculoskeletal problems (3.0%), compared to no reported adverse events in the control groups (n=155). Specifically, 2 subjects withdrew from the exercise intervention due to training-related back pain (73;151). Some subjects complained of transient muscle strength reduction (n=3) at the beginning of the exercise program (25;71;151) or expressed worsening fatigue (n=2) (22;23), but all subjects were able to complete the intervention.

What Types of Adverse Events Were Associated With Exercise Interventions in People With Spinal Cord Injury?

Muscle pain was the most commonly reported adverse event in people with Spinal Cord Injury who participated in an exercise intervention. Among 208 subjects, 4 (1.9%) experienced muscle pain during the aerobic training sessions (77) or after isokinetic testing (31). None of these complications affected their ability to complete the exercise program. One study (77) noted that exercise did not worsen the skin health of people with Spinal Cord Injury, and in 2 of 4 subjects who had pressure sores not associated with the exercise intervention, they healed by the completion of the study. One RCT reported that exercise using an arm ergometer in the supine position caused one participant (0.5%) to have bladder spasms (28).

What Types of Complications Were Associated With Exercise Interventions in People With Cerebral Palsy?

In the 11 reviewed studies involving 123 subjects in the exercise group and 69 subjects in the control group, no studies reported any complications in individuals with Cerebral Palsy, and only one study reported that a 6-week strengthening exercise intervention had negatively affected self-concept in children with Cerebral Palsy, but the reasons behind the unexpected reduction were unclear (152).

Is It Safe for Older Adults With Alzheimer's Disease To Exercise?

The major concern regarding exercise interventions for older persons with Alzheimer's disease is risk of falls. Among 229 individuals with Alzheimer's disease in 6 different exercise trials in which the primary exercise mode was walking, one study reported that there was no difference in the incidence of falls over a one year period between the exercise and control group referred to as the routine medical care group (139 versus 136) (106).

Is It Safe for People With Parkinson's Disease To Exercise?

In the 14 exercise interventions reviewed consisting of 287 subjects in the exercise condition and 183 subjects in the control condition, no adverse events related to the exercise exposure in people with Parkinson's disease occurred. In one study that was conducted to determine whether high-force eccentric resistance exercise caused subjects with Parkinson's disease muscle damage to their lower extremity, the researchers noted that the exercise exposure did not have a negative impact on muscle damage or function (75).

Is It Safe for People With Mental Illness or Intellectual Disability/Down Syndrome To Exercise?

Mental Illness

In the 15 studies that addressed the effects of exercise in participants with major depression disorder (n=335), only 2 RCTs reported adverse events related to the exercise exposure.

These included musculoskeletal injuries (n=8, 2.4%), chest pain (n=1, 0.3%), and increased severity of depressive symptoms (n=1, 0.3%) (54;144). One study concluded that compared to medication use, subjects in a treadmill exercise program experienced a lower incidence of diarrhea or loose stools (21% for those exercising at home and 10% in supervised exercise group) compared to those in the antidepressant group (31%) (53). Further, no adverse events related to exercise training were reported in 135 participants who were diagnosed with schizophrenia and bipolar disorder (n=11). Among all control group participants (n=210), no reported adverse events occurred.

Intellectual Disability

In the 12 exercise trials involving persons with Intellectual Disability including Down syndrome, none of the studies reported any physical complications. Only one trial reported that swimming in an integrated environment caused negative effects on perceived athletic competence for youth with intellectual disability compared to a segregated swimming class, although the swimming performance of subjects in the integrated setting increased (153).

Overall Summary and Conclusions

This report systematically evaluated published evidence regarding the effects of physical activity on people with physical and cognitive disabilities. Table G11.19 presents the findings in aggregate form, collapsing all physical disabilities into one group and cognitive disabilities into another group. Aggregating these data allows for a summary of the changes associated with exercise by health outcome and disability group (physical versus cognitive).

To determine the strength of evidence, each health outcome across the 6 categories evaluated in this report was identified and categorized by level of evidence according to the following criteria: Strong: 75% or more of reviewed trials had significant findings; Moderate: 50% to 74% of reviewed trials had significant findings; Limited: less than 49% of reviewed trials had significant findings. Two or more studies with significant findings on the identified health outcome were required for classification into strong or moderate level of evidence. Based on this classification scheme, for people with physical disabilities there was strong evidence that exercise can increase cardiorespiratory, musculoskeletal and mental health outcomes; moderate evidence to improve a variety of functional health outcomes and reduce the effects of certain types of secondary conditions (i.e., pain and fatigue associated with the primary disability); and limited evidence in improving healthy weight and metabolic health. For people with cognitive disabilities, there was strong evidence that exercise can improve musculoskeletal health, select functional health and mental health outcomes; moderate evidence for improving cardiorespiratory, musculoskeletal, and healthy weight and metabolic health; and limited evidence for reducing secondary conditions.

Table G11.19. Summary Table on Level of Evidence by Health Outcome Aggregated by Physical and Cognitive Disabilities

Health Outcome:	Significant Number of Trials	Significant Percent	Non-Significant Number of Trials	Non-Significant Percent	Level of Evidence Strong	Level of Evidence Moderate	Level of Evidence Limited	Level of Evidence No Evidence
Physical Disability: Cardiorespiratory Health	33	84.6%	6	15.4%	●	–	–	–
Physical Disability: Musculoskeletal Health	33	89.2%	4	10.8%	●	–	–	–
Physical Disability: Functional Health	50	63.3%	29	36.7%	–	●	–	–
Physical Disability: Secondary Conditions	10	71.4%	4	28.6%	–	●	–	–
Physical Disability: Healthy Weight and Metabolic Health	4	30.8%	9	69.2%	–	–	●	–
Physical Disability: Mental Health	10	83.3%	2	16.7%	●	–	–	–
Cognitive Disability: Cardiorespiratory Health	8	72.7%	3	27.3%	–	●	–	–
Cognitive Disability: Musculoskeletal Health	4	80%	1	20%	●		–	–
Cognitive Disability: Functional Health	10	83.3%	2	16.7%	●	–	–	–
Cognitive Disability: Secondary Conditions	1	100%	0	0%	–	–	●	
Cognitive Disability: Healthy Weight and Metabolic Health	4	50%	4	50%	–	●	–	–
Cognitive Disability: Mental Health	11	78.6%	3	21.4%	●	–	–	–

In summary, since the publication of the *Surgeon General's Report on Physical Activity and Health* in 1996 (154), a growing volume of research, including a number of RCTs, supports the use of physical activity to improve health and function among people with disabilities. With appropriate screening procedures, physical activity is considered to be a relatively safe, effective, and very important health recommendation for people with physical and cognitive disabilities. Data on select disability groups show improvements in various health outcomes including cardiorespiratory, musculoskeletal, functional, metabolic, and mental health, in addition to reducing certain secondary conditions associated with the primary disability such as pain and fatigue. An important caveat in interpreting these findings is that each study had its own prescreening evaluation for entrance into the study, which may have limited the sample to a select group of individuals within a certain range of health and function. Within this limitation, however, the consistency of the findings suggest that exercise training is an effective intervention for promoting health at a low risk of complications/adverse events in individuals with physical and cognitive disabilities.

This report also provides a framework for continuing to build an evidence base that can identify specific doses of physical activity in relation to key health outcomes in people with a variety of physical and cognitive disabilities. New studies and other disability groups can be added to the database as more research is published. In the future, in areas where data are lacking, researchers will be able to review the evidence and develop interventions that target key health outcomes in underserved groups of individuals with disabilities.

The development of appropriate inclusion/exclusion criteria is an important approach to ensuring that exercise is safe for a specific subgroup of people with disabilities. In all of the studies reviewed, screening and specific inclusion/exclusion criteria were important in terms of distinguishing individuals who were or were not appropriate for the intervention, usually based on level of current health or functional limitations. With younger, less disabled groups, risks associated with exercise appear to be typical of the general population. Given the high rate of physical inactivity reported among people with disabilities, it is critical for policymakers to promote physical activity guidelines among professional groups and associations that have regular contact with people who have disabilities (e.g., rehabilitation providers, fitness professionals, health care professionals, public health programs, service providers), and to support efforts to increase access to physical activity venues including indoor and outdoor sports, recreation and fitness facilities.

Safety of Exercise

This review also provides strong evidences that the benefits of physical activity for people with physical and cognitive disabilities far outweigh the risks. Very few reported serious adverse events (n=34, 1.15%). Although most of the studies were done in a controlled setting and may have excluded severely disabled subjects, the existing evidence supports the use of physical activity as a recommended health promoting activity among people with disabilities, including those with progressive disorders (i.e., multiple sclerosis) or more severe conditions (i.e., muscular dystrophy).

Limitations

This report does not account for differences in methodological quality. In the future, it would be helpful to qualify the RCTs based on selection criteria such as adequate sample size, equal groups (control and experimental) at baseline, blinding of study staff (i.e., different assessors for pre- and post-testing), recording of participant completion and dropout, and intention to treat. Studies were evaluated by their level of significance and not according to their effect sizes. We focused on 11 key disability groups only and did not include other disabled populations, such as those with rheumatoid arthritis, and populations in which disabilities occur at low incidences, such as those with spina bifida and polio, where not enough studies were available to include in this review.

All of the studies reviewed in this report had several outcomes (e.g., physical and emotional well being, reduced fatigue, increased fitness), and used a variety of interventions and doses of exercise (length of training, frequency, duration, intensity, modality). Several studies included individuals with a wide range of function and age, which may have attenuated the potential effects of the training regimen on certain subgroups within the larger sample (e.g., younger versus older subjects). Although heterogeneous populations make it easier to recruit subjects (e.g., using individuals with para- and tetraplegia in the same study) and obtain higher levels of statistical power, generalizability to the entire population (i.e., Spinal Cord Injury or Multiple Sclerosis) may be limited because of variations in health and function among the different subjects.

Another limitation was that the studies did not necessarily represent individuals with severe forms of the disability (i.e., tetraplegia versus paraplegia, severe cerebral palsy versus mild cerebral palsy; advanced types of multiple sclerosis). Therefore, it is not possible to generalize the findings to various subgroups within each disability who may have had an advanced condition. Data on certain subgroups (i.e., lower limb loss, cerebral palsy) also were limited, which reduced their generalizability.

Although we identified all the complications/adverse events reported in the 139 studies that were reviewed, it is possible that some of the studies did not report certain complications or adverse events.

Research Needs

It is important to identify optimal doses of exercise based on evidenced-based outcomes that delineate the safety of the activity and the specific health outcomes achieved by various exercise regimens for various disabled populations. The lack of data pertaining to the frequency, intensity, duration, and modality components of an exercise prescription for persons with disabilities has made it difficult to recommend specific training regimens to improve certain health outcomes or reduce the severity of certain secondary conditions associated with the disability (e.g., pain, fatigue).

The questions posed for this review suggest several lines of research to understand the dose-response effects of exercise in the treatment and management of targeted health outcomes. In order to establish a focused research agenda, studies should have an acceptable level of homogeneity (i.e., age, health status, functional level), and a consistent methodology, training dose and targeted outcome(s).

The very low exercise participation rate observed among people with disabilities may be associated with the gap between an individual's needs, interests and functional level, and the barriers that are often present in the environment. Environmental factors also can have a significant role in a person's ability to exercise, including access to exercise equipment or programs/classes, available transportation to and from the facility, and cost of the program. Collectively, these factors can make it extremely difficult for someone with a disability to participate in regular exercise. Health professionals must increase their awareness of the personal and environmental barriers that can have a substantial negative effect on participation in people with different types and severities of disabilities.

Specific Research Recommendations

1. There are no prospective cohort studies on people with disabilities. These studies should be conducted to determine the frequency, intensity, or duration of physical activity associated with key health outcomes, including reduction in certain secondary conditions associated with the specific disability subgroup (e.g., pain in spinal cord injury, fatigue in multiple sclerosis, deconditioning in intellectual disability). Studies should be stratified by age, functional level, and severity of disability.

2. The heterogeneity between and within disability groups and the low incidence of many disabilities make it extremely difficult to obtain an adequate sample size when recruiting from one setting. Multi-center clinical exercise trials are recommended to achieve adequate statistical power and to be able to generalize findings to certain subgroups within the targeted disability (e.g., young adults with paraplegia). A high level of intervention fidelity must be established that employs the same testing instruments, procedures and training regimen.

3. RCTs are needed to examine the effects of various *types* of exercise in addition to the actual training volume (frequency, intensity, duration). Group exercise such as tai chi or yoga may have the additional social benefit, which may improve outcomes but may also confound the benefit of the specific dose of exercise. Future studies should control for the social aspect of exercise in order to obtain accurate data on the exercise regimen itself versus the social benefits associated with exercising in a group.

4. Numerous self-report assessment tools have been developed to measure changes in health. It is difficult to make comparisons between studies when instruments are not the same or not explained well enough to make critical comparisons between them.

Given the small sample of many disabled subgroups, it would be helpful to have a recommended set of instruments for each targeted outcome with good psychometric properties so that data from various studies can be compared to each other.

5. Innovative strategies for recruiting individuals who generally do not volunteer for research studies must become a high priority. Because most experimental research is conducted with volunteers, it is difficult to generalize the study's findings to the entire subgroup. People who volunteer for exercise-related research may generally be younger and/or have a higher functional level. This is a common problem in experimental research but may be an even greater issue among people with disabilities because sample selection is limited to a small subset of the population and barriers such as transportation limit opportunities for participation in clinical research.

6. Several studies emphasized the unique aspects of improving social integration and/or quality of life. These measures are often obtained from self-report measures. It would be helpful to better understand how these measures are associated with objective measures, such as quantifying an increase in community participation (i.e., increased number of outdoor and/or social activities, greater amount of time outside the home for social events, increased employment). The fact that physical activity can improve mental health and quality of life is an intriguing concept that should be examined in future research with objective measurement of these outcomes.

7. Given the difficulty in identifying and recruiting subjects from certain populations with disabilities that have low incidence (e.g., spina bifida, muscular dystrophy, cerebral palsy), categorizing subjects by function rather than disability may be an alternative approach to increasing recruitment size and identifying key health outcomes that generalize across disability groups. Use of the International Classification of Functioning Disability and Health (ICF) (155) model would allow researchers to identify specific eligibility criteria by impairments (e.g., lower extremity paralysis) and/or activity limitations (e.g., unable to walk) rather than by disability.

Review of the Science: Physical Activity During Pregnancy and the Postpartum Period

Introduction

Early studies on physical activity and pregnancy were concerned more with harm to the mother and fetus than with potential benefits. Most studies used animal models, though some human studies examined cardiorespiratory responses and thermoregulation in the mother, fetal heart rate, and pregnancy outcomes such as birth weight, gestational length, and adverse events.

The American College of Obstetricians and Gynecologists (ACOG) developed the first exercise guidelines for pregnant women in 1985 (156). Those guidelines were based on limited data and were conservative. They included upper limits of 140 beats per minute for maternal heart rate and recommended that sessions of strenuous activity be limited to 15 minutes. The guidelines also noted the potential need to individualize physical activity recommendations.

Between 1985 and 1994, nearly 600 relevant studies were published, most of which focused on doing no harm. Many studies were laboratory investigations with small sample sizes, and most involved acute maternal responses to exercise. The data suggested no detrimental effects of the targeted exercise to mother or fetus, possible reduced length of labor, possible improvement in gestational diabetes, and relatively little loss of fitness by chronic exercisers. The use of a target heart rate was found to be quite problematic. ACOG updated its guidance for exercise during pregnancy in 1994 (157) and again 8 years later (158). Currently, ACOG recommends that pregnant women participate in 30 minutes of moderate-intensity physical activity on most days of the week in the absence of medical/obstetrical complications (158). Although this recommendation does not endorse participation in vigorous activities for all (for which information is scarce), it does not recommend against women being strenuously active during pregnancy.

Overview of Questions Asked

This part of the ***Understudied Populations*** section addresses 3 questions:

1. What does recent research indicate about the possible risks of moderate- or vigorous-intensity physical activity by women who are pregnant?
2. Does being physically active while pregnant provide any health benefits?
3. Does being physically active during the postpartum period provide any health benefits?

Data Sources and Process Used To Answer Questions

The evidence presented here was based on references included in the review of the literature for the 2006 Institute of Medicine report on physical activity and health (159) and an updated search of the Cochrane Library and MEDLINE for published RCTs, meta-analyses, and review articles. Search terms included exercise, physical activity, pregnancy, postpartum, the names of experts in the field and/or a combination of these terms. Search limits included human studies in women published in the English language from 1996 onward. Relevant articles were reviewed and the subcommittee's conclusions were summarized and presented here.

Question 1. What Does Recent Research Indicate About the Possible Risks of Moderate- or Vigorous-Intensity Physical Activity by Women Who Are Pregnant?

Moderate-intensity leisure-time physical activity is not associated with an increased risk of low birth weight, preterm delivery, or early pregnancy loss (160;161). A recent review concluded that moderate-intensity leisure-time physical activity during pregnancy normally does not affect birth weight. However, participation in vigorous activities has been associated with small reductions (about 200 to 400 grams) in birth weight compared to birth weights of babies born to less active women (160). Similar results were reported in a meta-analysis published in 2003 (162).

Information on strenuous activity during pregnancy is very limited. A prospective study in the United States found that participation in vigorous (6 or more METs) activities in the first and second trimesters was associated with non-significant risk reductions for preterm delivery (163). Similarly, a prospective Australian study found no significant effects of vigorous physical activity during pregnancy on gestational age at birth or birth weight (164). Results from these studies must be applied cautiously as only a select subset of pre-trained women chose to continue vigorous activity during pregnancy.

Question 2. Does Being Physically Active While Pregnant Provide Any Health Benefits?

In 2005, an expert panel was assembled to examine the impact of physical activity during pregnancy and the postpartum period on maternal chronic disease risk (165). The panel also addressed the association of physical activity with the risk of preeclampsia and gestational diabetes mellitus (GDM). Regular physical activity in early pregnancy has been found to be associated with a reduced risk of preeclampsia in 2 case-control studies (166;167) and one cohort study (168). The evidence is not strong, but is consistent. A more recent Cochrane Review of RCTs found a non-significant reduction in risk of preeclampsia associated with moderate physical activity during pregnancy; although only two trials with a combined sample size of 45 women met review criteria (169). A Cochrane Review for GDM also showed no significant effect of physical activity (170). However, reviews of observational studies consistently show a reduced risk of GDM associated with moderate physical activity participation before and/or during early pregnancy (160;171). Although conclusions from these reviews along with data from a large population-based prospective study (172) confirm that leisure-time physical activity reduces risk and helps to treat GDM, data are insufficient to develop specific optimal physical activity guidelines for GDM prevention.

Investigators also have evaluated maternal physical activity in relation to health-related fitness, psychological health, and the course of labor and delivery. The evidence clearly supports that maternal physical activity of any kind helps to maintain fitness levels, which normally decrease during pregnancy (161;173). Fewer studies have considered maternal mood during pregnancy, yet available evidence suggests that maternal physical activity improves mood and is associated with increased self-esteem (161;174). Conflicting results exist relating maternal physical activity to the course of labor and delivery. Some studies report easier and shorter deliveries, others find no effect, and some show that induction of labor is used more often among women who exercise (161). Variances in methodology and activity definitions make these studies difficult to summarize and compare. A recent study (175) showed that women who exercised during pregnancy were less likely to have preterm delivery compared to their sedentary counterparts. However, the authors were not able to clearly separate the role of moderate versus vigorous activity on this effect.

Question 3. Does Being Physically Active During the Postpartum Period Provide Any Health Benefits?

Available evidence has shown maternal physical activity during the postpartum period is associated with enhanced mood (165;176;177), increased cardiovascular fitness (177;178), and obesity prevention (179). Larson-Meyer (177) reviewed approximately 60 cross-sectional studies and RCTs on postpartum weight reduction, specifically, looking at postpartum exercise. When compared to no physical activity, moderate physical activity did not appear to increase postpartum weight reduction unless caloric restriction was included. Studies also have showed that moderate intensity aerobic exercise did not adversely affect milk volume, composition, or infant growth (165;177;180). Some longitudinal data on future disease risk come from Rooney and colleagues (179) who examined nearly 800 women immediately postpartum and again 15 years later. Disease and risk factor development (diabetes, heart disease, dyslipidemia, and hypertension) were directly related to weight gain over 15 years. Women who continued to perform aerobic exercise postpartum were less likely to become obese than those who did not. In summary, in the absence of medical complications, physical activity during the postpartum period is beneficial to the overall health of the mother (both in the short- and long-term) while not adversely affecting her newborn's development.

Overall Summary and Conclusion

Although the benefits of maternal physical activity have clearly been demonstrated, prospective, randomized intervention studies in diverse populations are greatly needed. Based on current evidence, unless there are medical reasons to the contrary, a pregnant woman can begin or continue a regular physical activity program throughout gestation, adjusting the frequency, intensity, and time as her condition warrants. Very little evidence exists for the dose of activity that confers the greatest health benefits to women during pregnancy and the postpartum period. In the absence of data, it is reasonable for women during pregnancy and the postpartum period to follow the moderate-intensity physical activity recommendations set for adults unless specific medical concerns warrant a reduction in activity. Habitual exercisers with high fitness levels undergoing a healthy pregnancy need not drastically reduce their activity levels, provided that they remain asymptomatic and maintain open communication with their health care providers so that adjustments can be made if necessary. This same communication should be continued into the postpartum period, where the time needed before a woman returns to performing regular physical activity should be governed by medical safety concerns, rather than a set time period.

Review of the Scientific Evidence: Racial and Ethnic Diversity

Introduction

The charge to the PAGAC by the Secretary of Health and Human Services was to review the science pertaining to physical activity and public health, including the literature that would help ensure that new federal physical activity guidelines and policy statements would apply to all Americans and, as best possible, also meet the needs of specific subgroups of the population.

Chronic disease risk and disease burden in the United States are higher in racial/ethnic minority communities than in non-Hispanic whites. Thus, special attention to the particular physical activity needs and requirements of these groups is warranted. To summarize the science addressing racial/ethnic specific health-related responses to various doses of physical activity, each subcommittee identified and reported data for specific racial/ethnic groups. The objective was to determine whether such responses significantly differed from those observed for non-Hispanic white men and women.

Compared to the large number of studies published since 1995 investigating the role of physical activity in disease prevention and health promotion, quite limited data exist on race-ethnic specific responses (181-185). Many studies have included only non-Hispanic white participants, or have included small sub-samples of other racial and ethnic groups, precluding meaningful sub-group analyses by race/ethnicity. Also limiting a comprehensive review of this issue is the failure of some authors to include (and editors to require) precise information on the racial/ethnic characteristics of the study populations (186). A few, mostly observational, studies have included data on several racial/ethnic populations or on one population other than non-Hispanic whites. Most of the latter have been studies conducted in countries other than the United States. The contexts for the physical activity-disease association in other countries may differ for similar populations living in the United States. However, studies in other countries provide a broader and more diverse perspective than may be obtained from US data alone.

Background

The public health burden imposed by physical inactivity may be disproportionately high in ethnic minority and lower SES communities (187-192). African Americans, American Indians/Alaska Natives, Asian Americans, Pacific Islanders, and Latinos have significantly lower levels of regular physical activity, and significantly higher levels of inactivity than do whites (6;193). Though Asian Americans and Pacific Islanders have traditionally been merged together in most data sets, disaggregation of these groups is critical because they tend to be at the opposite ends of the spectrum of body weight, which influences and is influenced by physical activity (Asian Americans have less, and Pacific Islanders, more obesity, compared to other population groups). Growing but smaller ethnic minority populations who are not always separately identified (e.g., South Asian and Middle Eastern), also likely experience challenges in achieving adequate physical activity participation (194). These differences are magnified by the recent data documenting the extremely low levels of objectively measured moderate-to-vigorous physical activity, and high levels of sedentariness, across the entire United States population, but especially among ethnic minorities (195;196).

Disparities exist in most physical activity-related chronic diseases and conditions. For example, overweight and obesity rates vary substantively by ethnicity, even taking into account SES (e.g., (197); (198), (199)). Despite the public health consensus that physical inactivity is an important determinant in a host of health disparities across population segments, racial/ethnic differences in the contribution of physical activity to various health outcomes have rarely been systematically investigated. Several reasons for possible differences have been postulated. There may be modest differences in the energy cost of physical activity, for example, as a result of racial anthropomorphic variations (see ***Part G. Section 4: Energy Balance*** for additional discussion). Alternatively, the dose response of physical activity on health outcomes may be similar across racial/ethnic populations, while cultural and contextual factors may lead to differences in the achieved effective dose of a particular intervention (implementation) or in the accuracy of a particular measure in capturing the dose delivered (evaluation).

The marked skewing of racial-ethnic minority populations toward lower SES compared with whites complicates interpretation of these observations of racial/ethnic differences in public health surveillance (200). SES explains some, but usually not all, racial/ethnic differences. In some studies, ethnicity was no longer significant when other sociodemographic variables reflecting SES were included in multivariate analyses of physical activity (185;201). In others, the magnitude of physical activity variation by ethnicity was statistically significant but much less substantive than variations related to other socio-demographic and health status characteristics (193;202).

This skewing makes it difficult, if not impossible, to examine the influence of SES independent of race/ethnicity on physical activity-related outcomes. In fact, because the data are so scant, heterogeneity between and within racial/ethnic groups generally limits extrapolation between studies. Inter-ethnic, and even intra-ethnic comparisons are further complicated because of the substantial confounding of race/ethnicity and SES. Lower SES non-Hispanic whites comprise a relatively low proportion of the white population overall, and are underrepresented in public health research. In contrast, substantial numbers and in some cases a majority of African American, Latino, Pacific Islander and American Indian study participants are of lower SES. As a result, inadequate sub-samples of lower income non-Hispanic whites or higher income ethnic minority participants hinder analytical disaggregation by race/ethnicity and SES. Therefore, we will focus on racial/ethnic differences, recognizing that race/ethnicity is, in part, a proxy measure for SES.

Overview of Questions Asked

This portion of the ***Understudied Populations*** section addresses one major question:

1. Is there evidence that the physical activity dose for improving health should vary for people depending on race or ethnicity?

Data Sources and Process Used To Answer Questions

A search of the *Physical Activity Guidelines for Americans* Scientific Database identified research articles on the effect of physical activity on racially/ethnically diverse groups. These articles were not readily identifiable within the database, as many articles retrieved using racial- or ethnic-specific keywords had very small minority samples and mention of racial/ethnic variations in outcomes were rare. Because so few relevant studies were available in the Database, pertinent reviews available through a MEDLINE search were considered, as were recently published and "in press" journal articles identified through reference lists of articles cited and through expert consultation.

Question 1. Is There Evidence That the Physical Activity Dose for Improving Health Should Vary by Race or Ethnicity?

Conclusions

Data addressing race- and ethnicity-specific responses to physical activity are still extremely limited. Very few subgroup analyses were reported that permitted direct comparisons between racial/ethnic groups. No clinically significant differences were identified in the review of studies comparing responses to physical activity between different racial or ethnic groups or in analyses adjusting for race and ethnicity. Data on various health outcomes in prospective observational studies involving populations other than non-Hispanic white men and women do not suggest any race- or ethnicity-specific responses to physical activity. However, too little evidence is available to draw firm conclusions. While additional data are being generated, the available evidence suggests that the major health benefits of physical activity are not race- or ethnicity-specific.

Rationale

Provided below is a brief summary of published research addressing the issue of race- and ethnicity-specific health-related responses to physical activity. For additional information about the health outcomes described here and for information about race/ethnicity data for other outcomes, the reader is referred to the remaining chapters in ***Part G: The Science***

Base. In general for these outcomes, data are insufficient to draw any conclusions regarding race- or ethnicity-specific effects or dose response.

All-Cause Mortality

Three studies included nationally representative samples of participants (203-205) and another comprised 48.3% blacks (206). In addition, 2 studies specifically enrolled Hispanics (207) and Japanese-American men (208). Five studies were conducted in Asia enrolling Chinese and Japanese subjects (209-213). No inter-ethnic/racial differences in the effect of physical activity on all-cause mortality were apparent.

Cardiorespiratory Health

Few studies conducted in the US have had an adequate sample size and clinical outcomes to evaluate the association between physical activity and cardiovascular disease (CVD) clinical events in race-ethnic groups other than non-Hispanic whites. An analysis of this issue in data from the Women's Health Initiative Observational Study (214) included 61,574 white women and 5,661 black women with a mean follow-up of 3.2 years. The relation between physical activity level (quintiles of MET-hours per week) and CVD clinical events was significant for both groups of women with relative risk (RR) for the highest versus lowest quintile of activity for white women being 0.56 (P for trend <0.001) and for black women 0.48 (P for trend = 0.02). In contrast to these results, a report on the Atherosclerosis Risk in Communities (ARIC) study population indicated that although there was a significant inverse relation between activity level and CVD clinical events in white men and women, no such relation was found for either black men or women (215). The authors suggest that this lack of association in blacks may be due to the limited number of blacks reporting vigorous physical activity (5% in black men versus 15% in white men). The different geographic locations of the black (primarily Mississippi) and white (Washington State, Minnesota, and North Carolina but not Mississippi) cohorts in ARIC may be relevant here. However, outside the United States where the relation between physical activity level and CVD clinical events has been evaluated in racial/ethnic populations other than whites, no indication exists that the favorable association frequently reported for non-Hispanic white men and women is absent. For example, physically active Japanese men and women living in Japan (216) and older Japanese men living in Hawaii (208) had lower CVD mortality rates than their least active counterparts. Similar results have been reported for Chinese women living in Shanghai (212) and Chinese men and women living in Hong Kong (210). In a case-control study that included men and women, conducted in New Delhi and Bangalore India, the RR for myocardial infarction of 145 or more MET-minutes per day of LTPA versus no activity was 0.44 (95% CI 0.27-0.41) and time spent in non-work sedentary activity also was directly associated with risk of myocardial infarction (RR for at least 215 minutes per day versus less than 70 minutes per day = 1.58 [95% CI: 1.05-2.36]). In an aerobic exercise training study lasting 20 weeks that included African-American and non-Hispanic white men and women, no racial-ethnic differences were observed in the percent increase in VO_{2max} (217).

Cancer

Within the United States, associations between increased physical activity and decreased breast cancer incidence have been observed in multiethnic populations (218-220) as well as in investigations in specific racial/ethnic minorities: black (219;221), Hispanic (220;222), and Asian American women (223). No differences in the magnitude or quality of this association were apparent.

Energy Balance

Twenty-four articles that included data on various racial-ethnic groups were identified during the systematic literature review. Half reported on studies conducted outside of the United States, including 9 in Asia/Pacific Islands, 2 in Africa, and 1 in Central America. Fourteen were cross-sectional studies (185;202;224-235), 3 were longitudinal cohort studies (201;231;236), and 7 were interventions (192;237-242). Only one of the intervention studies included a direct comparison between two racial-ethnic groups, whites and blacks (239). The actual body weight lost during the 20 weeks of exercise was the same for both groups – 0.2 kilogram – and this loss was statistically significant in whites but not blacks, most likely because of a lower statistical power for the blacks due to their much smaller sample size. It should also be noted that this was designed as an exercise training study and not a weight loss study. Also, adjustments for subtle racial/ethnic anthropomorphic variations that might explain any racial/ethnic differences (e.g., shorter trunk length in blacks), identified in experimental exercise physiology studies (243) were not reported (239).

Metabolic Disorders

Preventing the Metabolic Syndrome

The majority of studies with large sample sizes was either conducted in Europe or was composed of whites of American or European descent. Though some of the better studies were conducted in populations composed of both African Americans and non-Hispanic whites, no studies examined the physical activity-metabolic syndrome association in an African-American or Hispanic population only (244-246). Thus, limited data are available on the relation between physical activity or fitness and preventing metabolic syndrome in populations other than non-Hispanic whites. It should be noted that studies that used populations composed of both whites and African Americans, such as NHANES (cross-sectional) and CARDIA (prospective), showed a strong dose response between activity (or fitness) and prevention of metabolic syndrome (245;246).

Preventing Type 2 Diabetes

In observational studies that included women only, 3 large US cohort studies (247-250) all found that greater physical activity was associated with a lower incidence of diabetes. However, in one study, this relation was present only in white women and not in women of African-American, Hispanic or Asian descent (250). These findings await confirmation because the study may not have been powered to detect differences across all racial/ethnic groups. Results were based on self-report of diabetes diagnosis in the total population but were confirmed in a subset using blood samples and physician reports. Data from RCTs as well as observational studies suggest clearly that, overall, women and men benefit from increased levels of physical activity in terms of preventing type 2 diabetes. In the Diabetes Prevention Program (251), treatment effects did not differ significantly according to either sex or racial/ethnic group. Although participant numbers became too small for clear results when grouped by ethnicity, it appears that risk reduction compared with placebo was greater for the lifestyle group (both diet and physical activity were parts of this intervention) than for the group taking the common diabetes drug, Metformin in whites (50% versus 12%, respectively) and Hispanics (57% versus 2%, respectively) (252). In African Americans (42% versus 29%) and Native Americans (43% versus 42%), the lifestyle and Metformin groups showed more similar efficacy. For Asian Americans, Metformin showed a non-significantly greater reduction than intensive lifestyle intervention (62% versus 30%).

Overall Summary and Conclusions

Given the paucity of outcome-specific studies providing useful information about racial/ethnic minority populations, evidence of physical activity influences **across** content areas was assessed generally.

- Across studies, results indicate that physical activity is related to a host of health outcomes in racial/ethnic minority populations. The direction of the association is the same in all racial/ethnic groups for which data were examined, with physical activity generally exerting a protective effect.

- Across studies, findings suggest that no minimum threshold of effect exists, especially for chronically inactive people (i.e., the majority of American adults). The lack of minority racial/ethnic inclusiveness of the physical activity promotion research literature may actually underestimate effects of a given dose, as more advantaged participants may have less capacity to benefit from preventive interventions (ceiling effects) (253). Recently reported data support that engaging in some amount of physical activity is better than doing nothing, and higher amounts of physical activity are associated with greater benefits and a broader spectrum of benefits.

- Subgroup analyses permitting head-to-head inter-racial/-ethnic comparisons of the influence of physical activity were rare. The very limited data available provide no indication that dose response differs between racial/ethnic groups.

Research Needs

- An increased number of federally-funded studies should be powered to include sufficient representation of at least one racial/ethnic minority or lower SES population, with sufficient sample size to permit subgroup analyses by race/ethnicity or SES. Adequate sampling of at least one understudied group should take precedence over achieving population representative samples, which usually have inadequate sample sizes for inter-group comparisons. The latter requirement has been enforced by review committees for more than a decade, with little progress in identifying racial/ethnic variations in the spectrum or level of benefit of a given dose of physical activity. Requests to be excused from this requirement should have strong scientific justification. Strict exemption criteria should be established in advance, and then rigorously applied by scientific review committees as a part of their scrutiny of racial/ethnic group inclusion overall.

- Cultural proficiency of recruitment and retention approaches and adequacy of resources directed toward recruitment and retention should be scrutinized by grant review committee members with special expertise in this area, similar to the separate assessments of adequacy of study methods and analytical approaches by review committee statisticians.

- Federal program officers should manage and balance their portfolios to ensure that racial/ethnic differences in PA-related exposures and outcomes are under active investigation, using RFAs and other mechanisms to direct funding toward disparities examination and elimination.

- Journals should require reporting of race/ethnicity, sex and SES of samples in the abstract as well as the body of the text.

- Subgroup analyses should be requested by journal editors and reviewers when sample size is sufficient, and further data disaggregation encouraged, to examine interactions between sociodemographic characteristics, e.g., sex-ethnicity, SES-ethnicity.

- Abstraction databases should include search criteria that permit ascertainment of inclusiveness, i.e., subgroup analyses by race/ethnicity or SES.

- Specific research questions deserve particular emphasis, such as the precise role in weight maintenance of racial anthropomorphic variations in resting or activity-related energy metabolism (as opposed to or in concert with age or sex-related differences) or in body composition.

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Part H: Research Recommendations

Physical Activity Guidelines Advisory Committee (PAGAC) members were requested to consider the research needed to help resolve unanswered or inadequately answered questions they identified during their review of the science. Although a substantial amount of research on physical activity and health has been published since 1995, major gaps still exist in our knowledge needed to establish cause and effect for various health outcomes and to better define dose response, especially at the low and high ends of the activity spectrum. At the end of many of the chapters in ***Part G: The Science Base,*** authors have included a listing or discussion directed at needed research for specific health outcomes included in their review. This section initially focuses on some overarching recommendations that are applicable to many of the outcomes considered during the PAGAC review. Following these general recommendations are priority recommendations specific to the outcomes considered by each subcommittee.

Overarching Research Recommendations

Participant Diversity

One issue that became evident during the PAGAC review was the lack of data on selected subpopulations, especially various race/ethnic groups, persons of low socioeconomic status (SES), individuals with specific cognitive and physical disabilities, and obese persons. Some of these groups have been excluded from participation based on study eligibility/exclusion criteria (e.g., ability to walk at a moderate pace, read or speak English), or because study logistics precluded them from easily participating (e.g., travel distances, study visits during work hours). Since 1995, many studies that included women as subjects have been published. However, only a few have provided within-study comparisons of the impact of physical activity on health outcomes between the sexes.

Recommendations

- Because of the scientific and logistical challenges of including adequate-sized samples of multiple groups in a study conducted at one institution, well-designed and executed multi-center studies are needed in which each research site can have access to subjects who represent various specific understudied populations. This is critically important in providing investigators with opportunities to examine interactions between sociodemographic factors, particularly sex and race/ethnicity or SES, and physical activity in relation to health and to make inter-group comparisons.

- Funding agencies should support well-designed studies of individual understudied populations, especially race/ethnic minorities, persons of low SES, and individuals with physical and cognitive disabilities, so that major questions regarding the effects of exercise and effectiveness of physical activity interventions in each of these populations can be answered. If an organization funded a number of such studies with at least a core of shared measures, they would have a well-diversified research portfolio on understudied populations. Such an approach would more likely answer key questions than would an approach that requires each investigator to include relatively small numbers of understudied populations in their studies.

- Journal standards for peer-reviewed articles should require a reporting of the race/ethnicity (in addition to sex and age) of the sample and presentation of subgroup analyses by race/ethnicity and/or SES if sample sizes are sufficient, rather than simply treating these as co-variates and adjusting for them.

Dose Response

In each of the review chapters, the dose-response data currently available are summarized. Based on these reviews, it is apparent that major unanswered issues still exist in response to the question, "How much of what type of activity is enough to improve health?" To have sufficient statistical power to appropriately evaluate dose response in experimental studies, the overall sample size needs to be relatively large. In observational studies, it has been difficult to isolate parameters other than overall activity amount from data collected using questionnaires. Many experimental studies have used one level of physical activity as the intervention (usually that included in recent recommendations) and, consequently, evaluation of any dose-response effects must rely on post-hoc comparisons. Given that the number of dose-response questions that can be asked are nearly limitless when considering various activity characteristics (type, intensity, frequency, duration, amount/volume), possible health outcomes, and different populations, it is important that some priority be developed for which dose response questions are most important.

Recommendations

- Some recently published data indicate that physical activity of a lower intensity and/or smaller amount than is currently recommended may provide significant health benefits for chronically inactive or unfit adults (who comprise a large proportion of the American population aged 18 years and over) and older adults. Both experimental and observational studies are needed to answer a variety of questions about the nature of benefits provided and characteristics of dose required at the low end. The range of physical activity used in the intervention should include a dose below that currently identified in physical activity recommendations to evaluate its impact and the stability of this level of physical activity behavior over time.

- There remains a lack of data defining both the shape of the dose-response curve at the higher amounts and intensities of activity for most health outcomes and whether an upper limit of benefit exists. Most current recommendations focus on a minimal or target amount/intensity of activity that is consistent with much of the population receiving some benefit, but don't address questions of "optimal" or "maximal" benefit. Studies are need to clarify the amount of physical activity, defined by metabolic equivalent (MET)-minutes per week or some other measure, at which additional improvements in various health outcomes no longer occur or at which increases are negated by increased adverse medical events.

- To fill the gap in our knowledge about dose response, investigators should design and conduct studies that evaluate effects of the following variables at fixed volumes of physical activity: intensity, frequency, duration, and multiple bouts. Details related to these variables would allow more precise physical activity guidelines to be developed across the breadth of activity-related health outcomes.

- Reasonable evidence exists that activity accumulated in short bouts throughout the day can favorably alter selected biomarkers for cardiovascular and metabolic diseases and improve cardiorespiratory fitness. However, no evidence is available that such patterns of activity may be beneficial for musculoskeletal health. Experimental studies are needed to extend this research involving activity bouts of different durations, especially multiple bouts shorter than 10 minutes and a few long bouts per week (e.g., 2 x 75 minutes) on various health outcomes. Observational studies are needed using assessment methodologies that will allow accurate quantification of a range of types of activity in different population groups (e.g., abdominally obese, frail elderly) and an evaluation of the effect of accumulation of short bouts on clinical outcomes independent of activity intensity and amount.

Measurement Methodology

The ability of the PAGAC to draw strong conclusions for various outcomes was limited by the wide variety of questionnaires used to assess physical activity and numerous different approaches to data analysis and presentation.

Recommendations

- Uniform data collection is needed with respect to the type of physical activity (e.g., leisure-time, occupational) and physical activity characteristics (e.g., intensity, duration, amount).

- The Compendium of Physical Activity has been very useful in assigning standardized values of absolute intensity to a wide range of activities, but it should be updated and expanded to children and youth.

- During the past decade, technology that provides for the objective assessment of physical activity in relatively large groups of subjects has increased rapidly, especially through the use of motion sensors and physiological monitoring. These technologies have the potential to greatly improve the accuracy and reliability of physical activity assessment in free-living populations leading to a better understanding of health benefits and dose response. Development and evaluation of these technologies are needed for assessing populations with different activity profiles and sociodemographic characteristics.

- A much better understanding is needed on how the results of physical activity assessed by new objective measurement methods can be compared to data collected by commonly used questionnaires.

Physical Activity and Physical Fitness Surveillance

Physical activity surveillance of the US population has been provided by the Behavioral Risk Factor Surveillance System (http://www.cdc.gov/brfss/), the Youth Risk Behavior Surveillance System (http://www.cdc.gov/HealthyYouth/yrbs/index.htm), and the National Health and Nutrition Examination Survey (http://www.cdc.gov/nchs/nhanes.htm), but the information provided by these surveys remains quite limited. Also, longitudinal physical fitness assessment of most population groups in the United States is non-existent. Lack of these data prevents evidence-informed decisions regarding the contribution any change in physical activity has on various health outcomes, such as the rapid increasing incidence of obesity, metabolic syndrome, and type 2 diabetes (T2D).

Recommendations

- Surveillance of the total activity energy expenditure of representative samples of the US population needs to be implemented once appropriate assessment tools have been developed and validated. Such tools could include either questionnaires or new objective measurement technology, or a combination of the two.

- Special attention needs to be given to the surveillance of both the physical activity and physical fitness of the US population at both ends of the age spectrum — toddlers/children and the oldest adults. These groups constitute a substantial portion of the US population and receive unique benefits from being physically active, but no national surveillance system for physical activity or physical fitness data exist for them.

Systematic Reviews and Meta-Analyses

During literature reviews by the PAGAC, it became evident that, for selected health outcomes in various populations, a large number of studies have been published since 1995, but neither quantitative systematic reviews nor meta-analyses have been published. Such reviews would be very helpful in drawing conclusions about health benefits, modifiers of the effects of physical activity, and dose response.

Recommendations

- Experts investigating specific health outcomes from physical activity should assess the nature and volume of recent publications and determine whether quantitative reviews of the data would contribute to existing knowledge, help formulate guidelines and policy statements, and help set research priorities.

Research Recommendations of PAGAC Subcommittees

In the review chapters in ***Part G: The Science Base,*** each subcommittee highlighted areas in which data are lacking and provided guidance regarding research needs for specific populations and health outcomes. The following section provides a consolidation of the key recommendations from these chapters. The varying format and style of these recommendations reflects the different approaches that subcommittees took in identifying and articulating research needs in their topic areas.

All-Cause Mortality

- Empirical data are needed that are specific to minority populations – African Americans and Hispanics, in particular.

- Empirical data are needed that are specific to disabled populations, whether physically or intellectually disabled.

- Additional studies are needed to clarify whether all activities “count” equally, because limited data now suggest that vigorous-intensity activities are associated with additional risk reductions, beyond their contribution to total energy expended, when compared with moderate-intensity activities.

- Additional data are needed to help clarify the shape of the dose-response curve. An emphasis on two areas of data collection would be particularly useful: (1) uniform data collection to assess the same domains of physical activity (e.g., leisure-time, occupational, household, and/or commuting) across studies, and (2) collection of sufficient details on physical activity to assess different modes of exercise (e.g., aerobic versus strength training) as well as energy expenditure and intensity.

- Studies are needed to determine the point (if any) on the dose-response curve at which no further reduction in all-cause mortality occurs.

Cardiorespiratory Health

Studies are needed to answer the following questions:

- What is the time course of acquisition of the cardiovascular health benefits resulting from increases in habitual physical activity?
- What are the cardiovascular health benefits of varying exercise bout duration, frequency, and intensity, while controlling for total volume?
- What effects do daily exercise exposures accumulated in short bouts have on the acquired cardiovascular health benefits of habitual physical activity?
- What are the effects of resistance training on cardiovascular health and what is the nature of dose-response effects (varying intensity, bout volume, and frequency of programs)?
- Are there sex differences in cardiovascular health benefits of habitual physical activity when controlling for activity volume?
- What are the specific harmful effects of physical inactivity on cardiovascular health and what are the characteristics of the inactivity most likely to produce harm?
- What are the specific effects of aerobic training, resistance training, and a combination on selected biomarkers of vascular health, such as brachial artery flow mediated dilation? What are the dose-response effects?
- What are the main characteristics of an exercise program for preventing and treating peripheral arterial disease (PAD)? What are the exercise dose-response patterns, sex differences, exercise modality options, differential effects on diabetic patients with PAD, on asymptomatic patients and are biomarkers available to predict exercise responders?

Metabolic Health

- Available data indicate that regular physical activity is associated with reduced risk of metabolic syndrome. However, it is not clear whether physical activity and exercise can be used in treating or reversing metabolic syndrome, and additional studies will help to clarify this issue.
- Research is needed in diverse populations to determine whether the effects of physical activity across the range of metabolic health issues, including metabolic syndrome, T2D, type 1 diabetes (T1D), and gestational diabetes, differ with race and ethnicity.

- Further examination of the effects of physical activity on metabolic syndrome and T2D also is warranted to determine whether and how its effect differ in youth and adults.

- Additional research evaluating dose-response patterns of exercise in preventing diabetes and cardiovascular outcomes in diabetes would make a valuable contribution to the metabolic health literature.

- Randomized controlled trials (RCTs) are needed to examine the effects of exercise on treating T1D in children and adults. Good cardiovascular outcome data in response to physical activity in T1D is lacking and could potentially be obtained in adult-onset T1D.

- Clinical studies in post-exercise hypoglycemia are needed to further study the intermittent high-intensity exercise approach to prevention and to compare extra carbohydrate versus lower insulin-dosing approaches to treating T2D.

- Research is needed on several issues related to gestational diabetes. For example, RCTs are needed to determine whether physical activity can prevent gestational diabetes. It also would be useful to have additional dose-response data on the role of exercise and physical activity in treating gestational diabetes.

Energy Balance

- Additional large scale, multi-site RCTs are needed to more thoroughly characterize the dose response of physical activity on weight stability, weight loss, and body composition across a variety of population groups, especially for those in the normal body mass index range. Only a limited number of RCTs have addressed these outcomes. Large-scale multi-site RCTs would allow investigators to more effectively address issues related to susceptibility to weight gain or resistance to weight or fat loss that may vary by sex, race/ethnicity, and age. As mentioned in the overarching recommendations, various volumes should be evaluated within the same study design.

- Determine the most effective strategies for promoting and maintaining sufficient doses of physical activity to facilitate weight loss and/or weight stability. It is important to develop effective intervention strategies to promote and maintain the desired level of physical activity for weight loss and/or weight stability because adherence to this level of physical activity is currently less than optimal. Although some strategies have been shown to be effective for improving adherence to this level of physical activity, the success of these strategies has been demonstrated in limited samples and populations. Therefore, additional research in this area is needed.

- Determine how much physical activity is needed to prevent weight regain following weight loss. Most of the available literature related to this question is observational or has relied on retrospective analysis of self-selected and self-reported levels of physical activity. Use of state-of-the art technology and complete energy balance designs are absent from the literature. Specifically, it appears that no adequately powered studies of sufficient duration with randomization have been conducted to examine different levels of physical activity following weight loss.

- Determine the physical activity effects on total and regional fat loss from those of weight loss, per se, especially in those people very susceptible to weight gain in the current social environment and who thus may be most resistant to weight or fat loss with exercise. Additional RCTs are needed to distinguish physical activity effects from weight loss effect. In addition, the large-scale use of imaging techniques is necessary to distinguish between subcutaneous and visceral fat depots in their responsiveness to endurance and/or resistance training. The ability of studies to translate imaging findings into simple anthropometric measures such as the waist or the abdominal circumference would increase the clinical and personal utility of the research.

- More research is needed to establish the risks and benefits of various regimens of physical activity in men and women with a body mass index of 35 or greater.

Musculoskeletal Health

Bone Health

- Risk for osteoporotic fractures is strongly influenced both by bone fragility and by falling. Physical activity is the only therapeutic intervention that can both increase bone strength and reduce risk for falling. A large RCT of the effectiveness of physical activity versus anti-resorptive therapy (e.g., bisphosphonates) on the prevention of fractures is needed.

- Bone mineral density can be measured with a high degree of precision and remains the best predictor of risk for osteoporotic fracture. However, studies of animals provide evidence that small increases in bone mineral density in response to mechanical loading reflect very large increases in bone strength. Development of better technologies for the non-invasive assessment of bone strength in humans would provide additional insights into the relative effectiveness of physical activity to enhance bone strength and reduce fracture risk.

Joint Health

- Dose-response studies are needed to determine the optimal frequency, intensity and duration of physical activity associated with benefits (minimum dose) or increased symptoms (maximum dose) among adults with arthritis and other rheumatic conditions.

- Longitudinal studies of the relationship of lifetime accumulation of moderate physical activity, particularly walking, and incident arthritis of all types among the non-elite athlete population are needed. Special attention should be paid to adequately capture potentially confounding and mediating variables.

Muscle Quantity and Quality

- Studies of the specific modes of physical activity that are most effective in preventing the age-associated decline in skeletal muscle mass and function are needed, with a focus on whether age-related changes in other factors (e.g., nutritional, hormonal) are important mediators of the response.

- Investigations should identify the underlying mechanisms that limit the capacity for muscle hypertrophy in response to resistance exercise with advancing age.

Functional Health

- Design large RCTs to determine whether physical activity can prevent or delay the onset of functional limitations and/or role limitations in older adults. Few controlled trials have confirmed the strong evidence from observational trials that physical activity prevents or delays the onset of functional and/or role limitations. Given the problem of confounding in observational studies, large RCTs are needed.

- Determine the dose response of multi-modal activities on improving functional health and reducing falls. Evidence suggests that moderate-intensity, multi-modal interventions can help improve functional health and reduce falls. However, we do not know whether physical activity has a threshold or dose effect. Studies are needed to determine whether a threshold below the current recommendations exists and whether higher-intensity interventions are more or less effective than moderate-intensity interventions.

- Determine whether the dose-response effect is relevant to single component versus multi-modal interventions. We need to know the dose response for each component of multi-component interventions, not just the dose response for the total intervention. This would provide information on how to mix components to achieve maximal benefit for a given amount of time and would help clarify whether single-mode physical activity interventions would be as successful at improving functional health as multi-modal interventions. No trials have addressed this question. Most trials have included multi-modal interventions in older adults.

- Determine whether physical activity reduces injurious falls (e.g., falls that result in fractures) in older adults at risk of falls. Physical activity reduces falls in older adults at risk of falls; however, little is known about whether it can reduce injurious falls. An RCT is needed that has sufficient power to assess whether physical activity can reduce injurious falls.

Cancer

- Knowledge about the role of physical activity in reducing the risk of common cancers would benefit from additional evidence gathered from clinical trials. In the survivorship setting, clinical trials showing a benefit of physical activity interventions on reducing deaths, recurrences, and reducing the impact of late or long-term treatment effects also would make a valuable contribution to our understanding of the needs of this growing population.

- Studies are needed to clarify biological mechanisms linking physical activity to specific cancers in order to identify associations with less commonly studied cancers.

- Studies are needed to define the shape of the dose-response curve of the physical activity-cancer relation in order to determine the effect of low-intensity activities and accumulated bouts.

- Observational epidemiologic research is needed to identify the dose, type, and frequency of physical activity on risk of various cancer sites and subtypes, in addition to identifying the effect of physical activity on risk of specific cancers within particular population subgroups, including various races and ethnicities, ages, sexes, and groups at elevated risk of cancer.

Mental Health

- Additional prospective cohort studies and tightly controlled RCTs are needed, especially for anxiety and sleep disorders. Specifically:

  - Additional studies of under-represented groups and of people at high risk of mental health disorders are needed.

  - Selection of potential confounders specific to mental health risks need to be included in prospective cohort studies.

  - Reporting of adherence to and dropout from trials should be improved, particularly with respect to the impact on the trial's efficacy and likely population effectiveness.

  - Investigators should strive for convergence of subjective and objective measures of physical activity and should specify the social and environmental contexts in which physical activity occurs.

   - Valid outcome measures need to be selected, refined, and used uniformly.
   - Physical activity exposures and outcomes need to be measured frequently to permit investigators to model change.
   - It would be helpful to conduct additional RCTs comparing the effects of exercise with other preventive interventions.
   - Novel designs that distinguish social moderators and mediators of outcomes from experimental contamination (i.e., placebo effects) would make a valuable contribution to the field.

- Studies are needed that manipulate or directly compare standardized features of physical activity, including type, intensity, and timing, with the settings in which activity takes place (e.g., group versus solitary, community versus home, indoor versus outdoor).
- It would be helpful to accelerate the synergy between human brain imaging studies and neuroscience studies that use animal models of human disease. This improved synergy could help elucidate biological mechanisms underlying the benefits of physical activity to mental health. An increased emphasis on modeling of social-cognitive mediators of mental health outcomes and studies of gene-environment interactions also would be valuable additions to the field.

Youth

- Determine whether physical activity affects classroom behavior and academic achievement in children and adolescents.
- Determine whether physical activity affects depression, anxiety, and cognitive function in children and adolescents.
- Determine the types and amounts of physical activity that are needed to prevent the development of excessive adiposity during childhood and adolescence.
- Identify the optimal types and amounts of physical activity needed to maintain cardiorespiratory and metabolic health during childhood and adolescence.
- Establish the dose-response pattern for the relation between physical activity and bone health in children and adolescents.

Adverse Events

- Determine how one selects the initial increment (dose) of activity for individuals who have been inactive that will maximize continued participation and minimize adverse events. Recommendations have been vague about the amount of activity a person should initially select.

- Determine how a person should select the size and frequency of increments to an activity plan for a previously inactive individual that will maximize continued participation and minimize adverse events. Although a 10% increase per week has been suggested for youth and young adults, and a 2 to 4 week interval for older adults has been suggested, little research exists to support such suggestions.
- Determine the incidence and risk factors for adverse events associated with walking.
- Current literature suggests that risks may be unrelated to either total volume of walking or intensity (using elevated treadmills). These findings need to be substantiated in other settings and populations.
- Research is needed on the rate of adverse events in various populations resulting from participation in various modes of physical activity, including weight-bearing and resistance training.
- Research is needed to provide evidence-based answers to the following questions regarding pre-participation medical screening. Does a recommendation for people to develop an activity plan with a health care provider prevent adverse events? Does it reduce participation in physical activity? If the answer to both questions is yes, what is the balance at the population level? Are such recommendations justified for certain population subgroups? If so, which ones?

Understudied Populations

People With Disabilities

- Prospective cohort studies should be conducted to determine the frequency, intensity, and duration of physical activity associated with key health outcomes, including reduction in certain secondary conditions associated with the specific disability subgroup (e.g., pain in spinal cord injury, fatigue in multiple sclerosis, reconditioning in intellectual disability). Studies should be stratified by age, functional level, and severity of disability.
- Multi-center clinical exercise trials should be conducted to achieve adequate statistical power and to be able to generalize findings to certain subgroups within the targeted disabilities (e.g., young adults with paraplegia). A high level of intervention fidelity must be established that employs the same testing instruments, procedures and training regimen. The heterogeneity between and within disability groups and the low incidence of many disabilities make it extremely difficult to obtain an adequate sample size when recruiting from only one location.

- RCTs are needed to examine the effects of various types of exercise in addition to the actual training volume (frequency, intensity, duration). Group exercise such as tai chi or yoga may have additional social benefit, which may improve outcomes but may also confound the benefit of the specific dose of exercise. Future studies should control for the social aspect of exercise so as to obtain accurate data on the exercise regimen itself versus the social benefits associated with exercising in a group.

- Improved self-report assessment tools should be developed to measure changes in health in disabled populations. It is difficult to make comparisons between studies when instruments are not the same or not explained well enough to make critical comparisons between them. Given the small numbers of many disabled subgroups, it would be helpful to have a recommended set of instruments for each targeted outcome with good psychometric properties so that data from various studies can be compared.

- Development of new and innovative strategies for recruiting disabled individuals who generally do not volunteer for research studies must become a high priority. Because most experimental research is conducted with volunteers, it is difficult to generalize a study's findings to the entire subgroup. People who volunteer for exercise-related research may be younger and/or have a higher functional level than the broader population of people with disabilities.

- Determine how self-report measures of social integration and/or quality of life are associated with objective measures, such as quantifying an increase in community participation (i.e., increased number of outdoor and/or social activities, greater amount of time outside the home for social events, increased employment). The fact that physical activity can improve mental health and quality of life is an intriguing concept that should be examined in future research on disabled populations with a more objective and standardized measurement of these outcomes.

- Develop research designs that categorize subjects by function rather than disability to increase recruitment and identify key health outcomes that generalize across disability groups. Given the difficulty in identifying and recruiting certain populations whose disabilities have low incidence (e.g., spina bifida, muscular dystrophy, cerebral palsy), use of the International Classification of Functioning Disability and Health (ICF) model would allow researchers to identify specific eligibility criteria by impairments (e.g., lower extremity paralysis) and/or activity limitations (e.g., unable to walk) rather than by disability.

Women During Pregnancy and the Postpartum Period

- Additional RCTs are needed evaluating activity regimens with different dose patterns on the course of labor and delivery.

- RCTs are needed to determine whether physical activity will help prevent gestational diabetes.
- More research is needed on dose response looking at the role of exercise/physical activity in treating gestational diabetes.
- Studies to compare effects of physical activity during pregnancy and the postpartum period in diverse race-ethnic groups are needed.
- Research is needed to examine the effect of physical activity in reducing risk of T2D in women with a history of gestational diabetes.

Racial and Ethnic Diversity

- An increased number of Federally-funded studies should be powered to include sufficient representation of at least one ethnic/minority or lower SES population, with sufficient sample size to permit subgroup analyses by race/ethnicity or SES. Strict exemption criteria should be rigorously applied.
- Cultural proficiency of recruitment and retention approaches and adequacy of resources directed toward recruitment and retention should be scrutinized by grant review committee members with special expertise in this area, similar to the separate assessments of adequacy of study methods and analytical approaches by review committee statisticians.
- Federal program officers should manage and balance their portfolios to ensure that racial/ethnic differences in physical activity-related exposures and outcomes are under active investigation, and should use requests for applications (RFAs) and other mechanisms to direct funding toward disparities examination and elimination.
- Journals should require reporting of race/ethnicity, sex, and SES of samples in the abstract as well as the body of the text.
- Subgroup analyses should be requested when sample size is sufficient, and further data desegregation should be encouraged to examine interactions between sociodemographic characteristics, e.g., sex-ethnicity, SES-ethnicity.
- Abstraction databases should include search criteria that permit ascertainment of inclusiveness (i.e., subgroup analyses by race/ethnicity or SES).
- Specific research questions deserve particular emphasis, such as the precise role in weight maintenance of racial anthropomorphic variations in resting or activity-related energy metabolism (as opposed to or in concert with age- or sex-related differences) in body composition.

Subcommittee Assignments

Biographical Sketches

Physical Activity Guidelines Advisory Committee Subcommittee Assignments

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Cardiorespiratory Health	William E. Kraus, MD	William L. Haskell, PhD Judith G. Regensteiner, PhD	Jason D. Allen, PhD Brian D. Duscha, MS Joseph E. Donnelly, EdD George A. Kelley, DA Bruce Jones, MD, MPH JoAnn Manson, MD, DrPH, MPH	Janet E. Fulton, PhD
Metabolic Health	Judith G. Regensteiner, PhD	William L. Haskell, PhD William E. Kraus, MD	Timothy Church, MD, MPH, PhD Steven M. Haffner, MD Richard F. Hamman, MD, DrPH Amy G. Huebschman, MD Irene Schauer, MD, PhD	Harold W. (Bill) Kohl III, PhD
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Subcommittee	Chair	Members	Consultants	CDC Liaisons
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Biographical Sketches of the 2008 Physical Activity Guidelines Advisory Committee Members

William L. Haskell, PhD, Chair

Dr. Haskell is Professor of Medicine (Active Emeritus), Stanford University School of Medicine. He received his PhD in exercise physiology from the University of Illinois. Professor Haskell has spent 40 years conducting research investigating the effects of habitual physical activity on health and performance, especially in the areas of chronic disease prevention, cardiac rehabilitation, and assessment of physical activity in free-living populations. He is an author on more than 350 scientific articles, chapters, and books. In addition to this research experience, he has participated in the development of guidelines for physical activity and health by the American College of Sports Medicine (ACSM), American Heart Association (AHA), American College of Cardiology, National Institutes of Health (NIH), and the Centers for Disease Control and Prevention (CDC). His professional recognitions include an Honorary Doctor of Medicine from Linkoping University, (Sweden); Honorary Member, Order of the Horse Collar Knights, University of Kuopio (Finland); the Honor Award for lifetime achievement from the American College of Sports Medicine; Science Honor Award for 2007, the President's Council on Physical Fitness and Sports; and the Lifetime Achievement Award, University of California at Santa Barbara Alumni Association. He continues to be actively involved in physical activity and health research and development and dissemination of educational materials for health professionals and the public.

Miriam E. Nelson, PhD, Vice Chair

Dr. Nelson is Director of the John Hancock Center for Physical Activity and Nutrition and associate professor of Nutrition at the Friedman School of Nutrition Science and Policy at Tufts University. She is also an adjunct faculty member of Tufts University's Tisch College of Citizenship and Public Service. Dr. Nelson received her PhD in nutrition from Tufts University.

For the past 20 years, Dr. Nelson has been Principal Investigator of studies on exercise and nutrition supported by grants from the Federal government and private foundations. Her research has focused on midlife and older adult health, with an emphasis on women. She has directed and collaborated on many studies examining the effects of strength training, endurance exercise, and balance training on reducing risk and/or minimizing symptoms of chronic disease and functional decline. Key areas of interest include bone health, arthritis, frailty, type 2 diabetes, heart disease, obesity, and sarcopenia. Recently, Dr. Nelson chaired an ACSM/AHA committee to develop recommendations for physical activity for older adults. The report was published in 2007.

Dr. Nelson has been recognized for her scientific contributions by a number of organizations. Following her doctoral research, Dr. Nelson received an American Association for the Advancement of Science Congressional research fellowship, allowing her to work for Senator Patrick Leahy from Vermont on issues related to health and human services. In 1994, she was named a Brookdale National Fellow, an award given to future leaders in the field of aging. Dr. Nelson is also a fellow of the ACSM. She is a frequent writer and public speaker to consumer audiences on physical activity and health issues.

Rod K. Dishman, PhD

Dr. Dishman is Professor of Kinesiology and Adjunct Professor of Psychology at the University of Georgia. He received his PhD at the University of Wisconsin-Madison and has focused his research on neurobiological aspects of the mental health outcomes associated with physical activity and on behavioral determinants of physical activity. His research has been funded by the NIH, CDC, the AHA, and the United States Olympic Committee (USOC). Dr. Dishman is a fellow of the ACSM, the American Psychological Association, and the American Academy of Kinesiology and Physical Education. He has served as a consultant on exercise to the NIH, CDC, the Sports Medicine Council for the USOC, and the Olympic Prize subcommittee of the Medical Commission of the International Olympic Committee (IOC). Dr. Dishman was one of 22 founding members of the IOC's Olympic Academy of Sport Sciences. He was a contributor to *Physical Activity and Health: A Report of the Surgeon General* and was a member of the writing committee for the ACSM Position Stand, *The Recommended Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory and Muscular Fitness and Flexibility in Healthy Adults.*

Edward T. Howley, PhD

Dr. Howley received his PhD degree from the University of Wisconsin-Madison. He completed a 1-year postdoctoral appointment at Pennsylvania State University and then joined the faculty of the University of Tennessee, Knoxville (UTK). Dr. Howley taught classes in exercise physiology and in fitness testing and prescription, and has co-authored textbooks in both areas. He recently retired from UTK after 37 years of service and holds the rank of Professor Emeritus.

Dr. Howley's research interests include metabolic and hormonal responses to exercise, caloric cost of various physical activities, and the interaction of exercise and diet on weight loss. He has published more than 60 research articles.

Most of Dr. Howley's volunteer efforts have been with the ACSM. He was actively involved in the development of ACSM certification programs, was an associate editor of the 6th edition of the ACSM *Guidelines for Exercise Testing and Prescription,* and served as ACSM President in 2002-2003. He currently serves as Editor-in-Chief of ACSM's *Health & Fitness Journal* and chairs the program planning committee for the annual ACSM Health & Fitness Summit meeting. He also served as a member of the Science Board of the

President's Council on Physical Fitness and Sports (2005-2007). Dr. Howley worked at the local level as the co-chair of the East Tennessee 2 Step Healthy Weight Initiative, a 12-month collaboration between the University of Tennessee, the Knox County Health Department, and the East Tennessee Regional Health Office. In 2007, Dr. Howley was recognized for his contributions with the ACSM Citation Award.

Wendy M. Kohrt, PhD

Dr. Kohrt is Professor of Medicine in the Division of Geriatric Medicine at the University of Colorado Denver. Dr. Kohrt has conducted clinical intervention studies aimed at understanding the health benefits of physical activity in older people for more than 20 years. Her research focuses on reducing risk for chronic diseases and conditions, such as osteoporosis, type 2 diabetes, abdominal obesity, and physical disability. She established the Investigations in Metabolism, Aging, Gender, and Exercise (IMAGE) research group at the University of Colorado Denver, which has the mission to be a national leader in aging research focused on the prevention of disease and the maintenance of functional independence in old age. Dr. Kohrt chaired the writing committee for the 2004 ACSM Position Stand on *Physical Activity* and *Bone Health*. She also is an invited member of the Isis Fund Network on Musculoskeletal Health established by the Society for Women's Health Research.

William E. Kraus, MD

Dr. Kraus is Professor of Medicine in the Division of Cardiovascular Medicine; Professor, School of Nursing; and Assistant Professor of Cell Biology at Duke University. He obtained his AB in astronomy and astrophysics from Harvard College in 1977 and his MD from Duke University in 1983. One goal of his research is to understand the cellular signaling mechanisms underlying the normal adaptive responses of skeletal muscle to physiologic stimuli, such as occur in exercise conditioning, and to understand the abnormal maladaptive responses to pathophysiologic stimuli, such as occur in congestive heart failure, aging, and prolonged exposure to microgravity. Dr. Kraus also is Director for Clinical Research at the Duke Center for Living, a multidisciplinary treatment and research facility dedicated to the primary and secondary prevention of cardiovascular disease, and he is Medical Director of the Duke Cardiac Rehabilitation Program. Dr. Kraus is a Fellow of the AHA, the American College of Cardiology, and the ACSM. He is Chair of the AHA's Physical Activity Committee of the Nutrition, Physical Activity and Metabolism Council.

I-Min Lee, MBBS, ScD

Dr. Lee is Associate Professor of Medicine at Harvard Medical School and Associate Professor of Epidemiology at the Harvard School of Public Health. She was born in Malaysia, schooled there, and received her medical degree from the National University of Singapore. She received a master's degree in public health and a doctoral degree in epidemiology, both from the Harvard School of Public Health.

Dr. Lee's research interests focus on the role of physical activity in preventing chronic diseases, in enhancing longevity, and in women's health. She has published more than 190 scientific publications. She has served on several expert committees addressing physical activity and health, including the committee writing the 1996 report *Physical Activity and Health: A Report of the Surgeon General*, the committee writing the 7th edition of the ACSM's guidelines for exercise testing and prescription in 2006, and the CDC/World Health Organization Collaborating Center Committee on developing and disseminating global physical activity recommendations in 2008.

Additionally, Dr. Lee is on the Editorial Boards of *Medicine & Science in Sports & Exercise* and *Harvard Women's Health Watch.* Among the honors she has received for her work on physical activity and health are the Young Epidemiologist Award in 1999 by the Royal Society of Medicine, United Kingdom; and the William G. Anderson Award in 2007 from the American Alliance for Health, Physical Education, Recreation and Dance. She is an elected member of the American Epidemiological Society and a fellow of the ACSM.

Anne McTiernan, MD, PhD

Dr. McTiernan is a faculty member in the Division of Public Health Sciences and Director of the Prevention Center at the Fred Hutchinson Cancer Research Center in Seattle, Washington, and a Research Professor in the University of Washington Schools of Medicine and Public Health and Community Medicine. Dr. McTiernan's research focuses on identifying ways to prevent new or recurrent breast cancer and colorectal cancer, especially with physical activity, obesity prevention, and chemoprevention. She is Principal Investigator of several clinical trial and cohort studies investigating the associations among exercise, diet, body weight, hormones, chemoprevention agents, and risk of cancer incidence and prognosis. She is Principal Investigator of the Seattle Transdisciplinary Research on Energetics and Cancer (TREC) program, which includes more than 25 scientists conducting research on mechanisms linking obesity and inactivity with cancer, and on obesity prevention. Dr. McTiernan is an elected Fellow of the ACSM, the North American Association for the Study of Obesity, and the American College of Epidemiology. Dr. McTiernan has published widely in major medical journals and is lead author of the book, *Breast Fitness: An Optimal Exercise and Health Plan for Reducing Your Risk of Breast Cancer* and editor of *Cancer Prevention and Management Through Exercise and Weight Control*. She has served on several national and international health advisory boards and working groups, including those of the International Agency for Research on Cancer's *Handbook of Cancer Prevention Vol. 6: Weight Control and Physical Activity* and the American Cancer Society's *Guidelines for Nutrition and Physical Activity and Prevention of Cancer*.

Russell R. Pate, PhD

Dr. Pate received his BS from Springfield College and his master's and doctorate degrees from the University of Oregon. In 1974, he joined the faculty of the University of South Carolina, where he now serves as Associate Vice President for Health Sciences and Professor in the Department of Exercise Science, Arnold School of Public Health.

Dr. Pate is an exercise physiologist whose research focuses on physical activity and physical fitness in children and the health implications of physical activity. He has published more than 170 scholarly papers and has authored or edited 5 books. His research has been supported by the NIH, the CDC, the AHA, and several private foundations and corporations. He heads a research team that currently is conducting research on physical activity and physical activity interventions in preschool children and in middle school girls. He coordinated the development of the 1995 landmark recommendation on Physical Activity and Public Health by the CDC and ACSM. He served on the 2005 U.S. Dietary Guidelines Advisory Committee, and on the Institute of Medicine (IOM) panel that developed guidelines for the prevention of childhood obesity.

Dr. Pate has served in several leadership positions with the ACSM, and in 1993-1994 served as that organization's president. In 1996, he received the Citation Award from ACSM, and in 1999 he received the Alliance Scholar Award from the American Alliance for Health, Physical Education, Recreation and Dance.

Kenneth E. Powell, MD, MPH

Dr. Powell is a public health and epidemiologic consultant in Atlanta, Georgia. He holds degrees from Harvard College (AB), Northwestern University Medical School (MD), and Harvard School of Public Health (MPH), and received postgraduate clinical training in internal medicine at the University of Colorado and the University of Utah. He was an epidemiologist with the CDC for 25 years and with the Georgia Department of Human Resources for nearly 8 years. The relationship between physical activity and health has been an important theme during his career. He initiated the CDC's epidemiologic work in the area by leading a consolidation of the scientific literature and setting the public health research agenda. He also participated in the development of the first nationwide surveillance of physical activity and the development of the physical activity-related objectives for the US Department of Health and Human Services' (HHS) *Healthy People 2000*. He served on the Committee on Physical Activity, Health, Transportation, and Land Use and the Committee on Progress in Preventing Childhood Obesity for the IOM, and is a member of the Physical Activity Work Group for the Task Force for the Guide to Community Preventive Services. He is a Fellow of the American College of Physicians, American College of Epidemiology, and ACSM.

Judith G. Regensteiner, PhD

Dr. Regensteiner is a Professor in the Divisions of Internal Medicine and Cardiology in the School of Medicine at the University of Colorado Denver. She is Director of the Center for Women's Health Research at that university and has strong research interests in this area, especially with relevance to cardiovascular disease and diabetes. Her expertise is in cardiovascular physiology, functional assessment (exercise testing and questionnaire design/evaluation), and exercise training in people with chronic diseases. She has been Principal Investigator or Co-Investigator of several previous and ongoing large grants from the AHA, NIH, and American Diabetes Association (ADA) to assess exercise performance, functional capacity, and the effects of exercise training in persons with diabetes and peripheral arterial disease. In addition, she is Principal Investigator of the Building Interdisciplinary Careers in Women's Health program that is funded by a K12 award from NIH. She has been involved with the San Luis Valley Diabetes Study in non-diabetics and persons with impaired glucose tolerance. She also was an investigator in the Diabetes Prevention Program and is currently an investigator of the Look AHEAD study (both multicenter studies from NIH). She developed and validated the Low Level version of the Physical Activity Recall (LOPAR), which was used as a secondary outcome measure in the Diabetes Prevention Program. Dr. Regensteiner has been involved in writing a consensus statement for the ADA addressing the appropriate, evidence-based treatment of persons with diabetes and peripheral arterial disease and in developing for the AHA clinical data standards for treating peripheral arterial disease patients.

James H. Rimmer, PhD

Dr. Rimmer is Professor in the Department of Disability and Human Development, College of Applied Health Sciences, University of Illinois at Chicago, and Adjunct Professor in the Department of Physical Medicine and Rehabilitation at Northwestern University Feinberg School of Medicine and Rehabilitation Institute of Chicago. He is Director of two federally funded Centers, the National Center on Physical Activity and Disability (funded by CDC) and the Rehabilitation Engineering Research Center on Recreational Technologies and Exercise Physiology Benefiting Persons With Disabilities (funded by the National Institute on Disability and Rehabilitation Research). Dr. Rimmer's research has focused on the effects of physical activity and nutrition on reduction of secondary conditions, including obesity and deconditioning, in adults and youth with physical and cognitive disabilities. He has published more than 90 manuscripts and book chapters and given more than 100 invited presentations to national and international audiences on topics related to physical activity, health promotion, rehabilitation engineering, secondary conditions, and disability. He also is Principal Investigator of a 5-year NIH clinical trial examining the impact of the built environment on obesity in people with mobility disabilities. Dr. Rimmer was recently appointed by HHS Secretary Leavitt to the Board of Scientific Counselors of the Coordinating Center for Health Promotion of the CDC.

Antronette K. (Toni) Yancey, MD, MPH

Dr. Yancey is currently Professor, Department of Health Services, and Principal Investigator of the CDC-funded Center of Excellence in the Elimination of Disparities, University of California at Los Angeles (UCLA) School of Public Health. She returned to academia full time in 2001 after 5 years in public health practice, first as Director of Public Health, Richmond, Virginia, and, subsequently, as Director of Chronic Disease Prevention and Health Promotion, Los Angeles County Department of Health Services. Dr. Yancey has authored more than 100 scientific publications, including 70 refereed journal articles and editorials. She also has been Principal Investigator on 4 NIH independent investigator (R01, R24) grants. Dr. Yancey's work has been cited by the *New York Times,* the *Los Angeles Times,* ABC, NBC, CBS, NPR, and many other media outlets nationally and internationally. She serves on the AHA Physical Activity Subcommittee, and until recently, on the Advisory Committee to the Director of the CDC and the IOM committee authoring the report, *Progress in Preventing Childhood Obesity: How Do We Measure Up?* She chairs the Board of Directors of the California-based Public Health Institute. In 2005, Dr. Yancey was awarded the California Public Health Association's first Health Promotion Award.
Dr. Yancey received her BS in biochemistry and molecular biology from Northwestern University and her MD from Duke University. She completed her preventive medicine residency and MPH at UCLA.