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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.

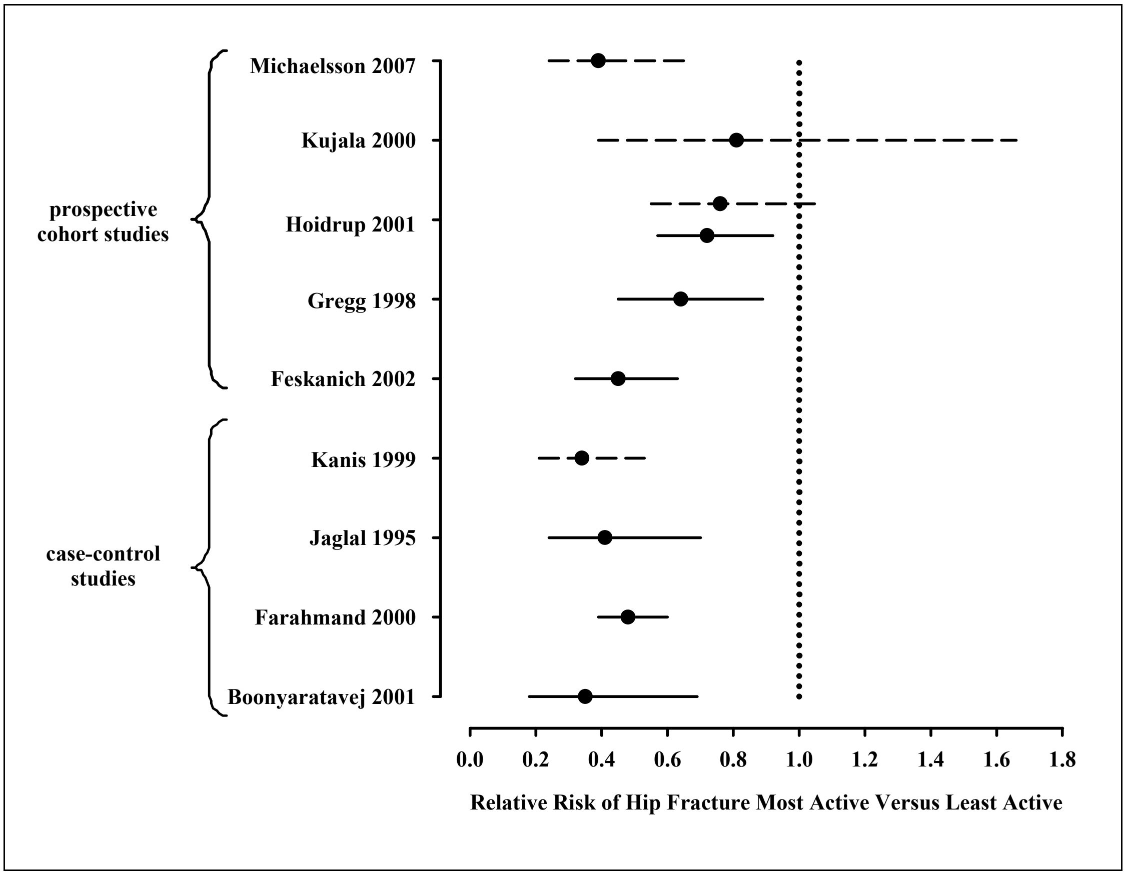
Type of Fracture

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.

Reference List

1. American Geriatrics Society, British Geriatrics Society, American Academy of Orthopaedic Surgeons Panel on Falls Prevention. Guideline for the prevention of falls in older persons. J.Am.Geriatr.Soc. 2001 May 12;49(5):664-72.

2. National Osteoporosis Foundation., American Academy of Orthopaedic Surgeons. Physician's guide to prevention and treatment of osteoporosis. Washington, D.C.: National Osteoporosis Foundation; 2003.

3. Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, Macera CA, Castaneda-Sceppa C. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. Med.Sci.Sports Exerc. 2007 Aug;39(8):1435-45.

4. Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, Gabriel S, Hirsch R, Hochberg MC, Hunder GG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum. 2008 Jan;58(1):26-35.

5. Wolfe RR. The underappreciated role of muscle in health and disease. Am.J.Clin.Nutr. 2006;84(3):475-82.

6. Feskanich D, Willett W, Colditz G. Walking and leisure-time activity and risk of hip fracture in postmenopausal women. JAMA 2002 Nov 13;288(18):2300-6.

7. Gregg EW, Cauley JA, Seeley DG, Ensrud KE, Bauer DC. Physical activity and osteoporotic fracture risk in older women. Study of Osteoporotic Fractures Research Group. Ann.Intern.Med. 1998 Jul 15;129(2):81-8.

8. Hoidrup S, Sorensen TI, Stroger U, Lauritzen JB, Schroll M, Gronbaek M. Leisure-time physical activity levels and changes in relation to risk of hip fracture in men and women. Am.J.Epidemiol. 2001 Jul 1;154(1):60-8.

9. Kujala UM, Kaprio J, Kannus P, Sarna S, Koskenvuo M. Physical activity and osteoporotic hip fracture risk in men. Arch.Intern.Med. 2000 Mar 13;160(5):705-8.

10. Thorpe DL, Knutsen SF, Beeson WL, Fraser GE. The effect of vigorous physical activity and risk of wrist fracture over 25 years in a low-risk survivor cohort. J.Bone Miner.Metab 2006;24(6):476-83.

11. Herala M, Kivela SL, Honkanen R, Koski K, Laippala P, Luukinen H. Recent decline in heavy outdoor work activity predicts occurrence of fractures among the home-dwelling elderly. Osteoporos.Int. 2002 Jan;13(1):42-7.

12. Roy DK, O'Neill TW, Finn JD, Lunt M, Silman AJ, Felsenberg D, Armbrecht G, Banzer D, Benevolenskaya LI, Bhalla A, et al. Determinants of incident vertebral fracture in men and women: results from the European Prospective Osteoporosis Study (EPOS). Osteoporos.Int. 2003 Jan;14(1):19-26.

13. Michaelsson K, Olofsson H, Jensevik K, Larsson S, Mallmin H, Berglund L, Vessby B, Melhus H. Leisure physical activity and the risk of fracture in men. PLoS.Med. 2007 Jun;4(6):e199.

14. Nguyen TV, Eisman JA, Kelly PJ, Sambrook PN. Risk factors for osteoporotic fractures in elderly men. Am.J.Epidemiol. 1996 Aug 1;144(3):255-63.

15. Joakimsen RM, Fonnebo V, Magnus JH, Stormer J, Tollan A, Sogaard AJ. The Tromso Study: physical activity and the incidence of fractures in a middle-aged population. J.Bone Miner.Res. 1998 Jul;13(7):1149-57.

16. Samelson EJ, Hannan MT, Zhang Y, Genant HK, Felson DT, Kiel DP. Incidence and risk factors for vertebral fracture in women and men: 25-year follow-up results from the population-based Framingham study. J.Bone Miner.Res. 2006 Aug;21(8):1207-14.

17. Greendale GA, Barrett-Connor E, Edelstein S, Ingles S, Haile R. Lifetime leisure exercise and osteoporosis. The Rancho Bernardo study. Am.J.Epidemiol. 1995 May 15;141(10):951-9.

18. Farahmand BY, Persson PG, Michaelsson K, Baron JA, Alberts A, Moradi T, Ljunghall S. Physical activity and hip fracture: a population-based case-control study. Swedish Hip Fracture Study Group. Int.J.Epidemiol. 2000 Apr;29(2):308-14.

19. Silman AJ, O'Neill TW, Cooper C, Kanis J, Felsenberg D. Influence of physical activity on vertebral deformity in men and women: results from the European Vertebral Osteoporosis Study. J.Bone Miner.Res. 1997 May;12(5):813-9.

20. Stevens JA, Powell KE, Smith SM, Wingo PA, Sattin RW. Physical activity, functional limitations, and the risk of fall-related fractures in community-dwelling elderly. Ann.Epidemiol. 1997 Jan;7(1):54-61.

21. Boonyaratavej N, Suriyawongpaisal P, Takkinsatien A, Wanvarie S, Rajatanavin R, Apiyasawat P. Physical activity and risk factors for hip fractures in Thai women. Osteoporos.Int. 2001;12(3):244-8.

22. Jaglal SB, Kreiger N, Darlington GA. Lifetime occupational physical activity and risk of hip fracture in women. Ann.Epidemiol. 1995 Jul;5(4):321-4.

23. Kanis J, Johnell O, Gullberg B, Allander E, Elffors L, Ranstam J, Dequeker J, Dilsen G, Gennari C, Vaz AL, et al. Risk factors for hip fracture in men from southern Europe: the MEDOS study. Mediterranean Osteoporosis Study. Osteoporos.Int. 1999;9(1):45-54.

24. Sinaki M, Itoi E, Wahner HW, Wollan P, Gelzcer R, Mullan BP, Collins DA, Hodgson SF. Stronger back muscles reduce the incidence of vertebral fractures: a prospective 10 year follow-up of postmenopausal women. Bone 2002 Jun;30(6):836-41.

25. Ringsberg KA, Gardsell P, Johnell O, Josefsson PO, Obrant KJ. The impact of long-term moderate physical activity on functional performance, bone mineral density and fracture incidence in elderly women. Gerontology 2001 Jan;47(1):15-20.

26. Nordstrom A, Karlsson C, Nyquist F, Olsson T, Nordstrom P, Karlsson M. Bone loss and fracture risk after reduced physical activity. J.Bone Miner.Res. 2005 Feb;20(2):202-7.

27. Holloszy JO, Kohrt WM. Exercise. In: Masoro EJ, editor. Aging. New York: Oxford University Press; 1995. p. 633-66.

28. Turner CH, Robling AG. Designing exercise regimens to increase bone strength. Exerc.Sport Sci.Rev. 2003 Jan;31(1):45-50.

29. Mashiba T, Turner CH, Hirano T, Forwood MR, Johnston CC, Burr DB. Effects of suppressed bone turnover by bisphosphonates on microdamage accumulation and biomechanical properties in clinically relevant skeletal sites in beagles. Bone 2001 May;28(5):524-31.

30. Hirano T, Burr DB, Turner CH, Sato M, Cain RL, Hock JM. Anabolic effects of human biosynthetic parathyroid hormone fragment (1-34), LY333334, on remodeling and mechanical properties of cortical bone in rabbits. J.Bone Miner.Res. 1999 Apr;14(4):536-45.

31. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, Macera CA, Heath GW, Thompson PD, Bauman A. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Med.Sci.Sports Exerc. 2007 Aug;39(8):1423-34.

32. U.S.Department of Health and Human Services and U.S.Department of Agriculture. Dietary Guidelines for Americans. 6th ed. Washington, D.C.: U.S. Government Printing Office; 2005.

33. Kohrt WM, Bloomfield SA, Little KD, Nelson ME, Yingling VR. American College of Sports Medicine Position Stand: physical activity and bone health. Med.Sci.Sports Exerc. 2004 Nov;36(11):1985-96.

34. Kelley GA, Kelley KS. Efficacy of resistance exercise on lumbar spine and femoral neck bone mineral density in premenopausal women: a meta-analysis of individual patient data. J.Womens Health (Larchmt.) 2004 Apr;13(3):293-300.

35. Kelley GA, Kelley KS. Exercise and bone mineral density at the femoral neck in postmenopausal women: a meta-analysis of controlled clinical trials with individual patient data. Am.J.Obstet.Gynecol. 2006 Mar;194(3):760-7.

36. Kelley GA, Kelley KS, Tran ZV. Exercise and lumbar spine bone mineral density in postmenopausal women: a meta-analysis of individual patient data. J.Gerontol.A Biol.Sci.Med.Sci. 2002 Sep;57(9):M599-M604.

37. Martyn-St James M, Carroll S. Progressive high-intensity resistance training and bone mineral density changes among premenopausal women: evidence of discordant site-specific skeletal effects. Sports Med. 2006;36(8):683-704.

38. Martyn-St James M, Carroll S. High-intensity resistance training and postmenopausal bone loss: a meta-analysis. Osteoporos.Int. 2006;17(8):1225-40.

39. Wolff I, van Croonenborg JJ, Kemper HC, Kostense PJ, Twisk JW. The effect of exercise training programs on bone mass: a meta-analysis of published controlled trials in pre- and postmenopausal women. Osteoporos.Int. 1999;9(1):1-12.

40. Wallace BA, Cumming RG. Systematic review of randomized trials of the effect of exercise on bone mass in pre- and postmenopausal women. Calcif.Tissue Int. 2000 Jul;67(1):10-8.

41. Kelley GA, Kelley KS, Tran ZV. Resistance training and bone mineral density in women: a meta-analysis of controlled trials. Am.J.Phys.Med.Rehabil. 2001 Jan;80(1):65-77.

42. Berard A, Bravo G, Gauthier P. Meta-analysis of the effectiveness of physical activity for the prevention of bone loss in postmenopausal women. Osteoporos.Int. 1997;7(4):331-7.

43. Kelley G. Aerobic exercise and lumbar spine bone mineral density in postmenopausal women: a meta-analysis. J.Am.Geriatr.Soc. 1998 Feb;46(2):143-52.

44. Lee MS, Pittler MH, Shin BC, Ernst E. Tai chi for osteoporosis: a systematic review. Osteoporos.Int. 2007 Oct 23.

45. Kelley GA, Kelley KS, Tran ZV. Exercise and bone mineral density in men: a meta-analysis. J.Appl.Physiol 2000 May;88(5):1730-6.

46. Kelley GA. Exercise and regional bone mineral density in postmenopausal women: a meta-analytic review of randomized trials. Am.J Phys.Med.Rehabil. 1998 Jan;77(1):76-87.

47. Palombaro KM. Effects of walking-only interventions on bone mineral density at various skeletal sites: a meta-analysis. J Geriatr.Phys.Ther. 2005;28(3):102-7.

48. Kelley GA. Aerobic exercise and bone density at the hip in postmenopausal women: a meta-analysis. Prev.Med. 1998 Nov;27(6):798-807.

49. Cussler EC, Going SB, Houtkooper LB, Stanford VA, Blew RM, Flint-Wagner HG, Metcalfe LL, Choi JE, Lohman TG. Exercise frequency and calcium intake predict 4-year bone changes in postmenopausal women. Osteoporos.Int. 2005 Dec;16(12):2129-41.

50. Huuskonen J, Vaisanen SB, Kroger H, Jurvelin JS, Alhava E, Rauramaa R. Regular physical exercise and bone mineral density: a four-year controlled randomized trial in middle-aged men. The DNASCO study. Osteoporos.Int. 2001;12(5):349-55.

51. Maddalozzo GF, Snow CM. High intensity resistance training: effects on bone in older men and women. Calcif.Tissue Int. 2000;66(6):399-404.

52. McCartney N, Hicks AL, Martin J, Webber CE. A longitudinal trial of weight training in the elderly: continued improvements in year 2. J.Gerontol.A.Biol.Sci.Med.Sci. 1996;51(6):B425-B433.

53. Stewart KJ, Bacher AC, Hees PS, Tayback M, Ouyang P, Jan de BS. Exercise effects on bone mineral density relationships to changes in fitness and fatness. Am.J.Prev.Med. 2005 Jun;28(5):453-60.

54. Woo J, Hong A, Lau E, Lynn H. A randomised controlled trial of Tai Chi and resistance exercise on bone health, muscle strength and balance in community-living elderly people. Age Ageing 2007 May;36(3):262-8.

55. Cussler EC, Lohman TG, Going SB, Houtkooper LB, Metcalfe LL, Flint-Wagner HG, Harris RB, Teixeira PJ. Weight lifted in strength training predicts bone change in postmenopausal women. Med.Sci.Sports Exerc. 2003 Jan;35(1):10-7.

56. Cooper C, Snow S, McAlindon TE, Kellingray S, Stuart B, Coggon D, Dieppe PA. Risk factors for the incidence and progression of radiographic knee osteoarthritis. Arthritis Rheum. 2000 May;43(5):995-1000.

57. Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, Kington RS, Lane NE, Nevitt MC, Zhang Y, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. Ann.Intern.Med. 2000 Oct 17;133(8):635-46.

58. Felson DT, Zhang Y. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. Arthritis Rheum. 1998 Aug;41(8):1343-55.

59. Felson DT. Risk factors for osteoarthritis: understanding joint vulnerability. Clin.Orthop.Relat Res. 2004 Oct;(427 Suppl):S16-S21.

60. Issa SN, Sharma L. Epidemiology of osteoarthritis: an update. Curr.Rheumatol.Rep. 2006 Feb;8(1):7-15.

61. Lane NE, Buckwalter JA. Exercise and osteoarthritis. Curr.Opin.Rheumatol. 1999 Sep;11(5):413-6.

62. Manninen P, Riihimaki H, Heliovaara M, Suomalainen O. Physical exercise and risk of severe knee osteoarthritis requiring arthroplasty. Rheumatology.(Oxford) 2001 Apr;40(4):432-7.

63. Foley S, Ding C, Cicuttini F, Jones G. Physical activity and knee structural change: a longitudinal study using MRI. Med.Sci.Sports Exerc. 2007 Mar;39(3):426-34.

64. Hanna F, Teichtahl AJ, Bell R, Davis SR, Wluka AE, O'Sullivan R, Cicuttini FM. The cross-sectional relationship between fortnightly exercise and knee cartilage properties in healthy adult women in midlife. Menopause. 2007 Sep;14(5):830-4.

65. Racunica TL, Teichtahl AJ, Wang Y, Wluka AE, English DR, Giles GG, O'Sullivan R, Cicuttini FM. Effect of physical activity on articular knee joint structures in community-based adults. Arthritis Rheum. 2007 Oct 15;57(7):1261-8.

66. Roos EM, Dahlberg L. Positive effects of moderate exercise on glycosaminoglycan content in knee cartilage: a four-month, randomized, controlled trial in patients at risk of osteoarthritis. Arthritis Rheum. 2005 Nov;52(11):3507-14.

67. Felson DT, Niu J, Clancy M, Sack B, Aliabadi P, Zhang Y. Effect of recreational physical activities on the development of knee osteoarthritis in older adults of different weights: the Framingham Study. Arthritis Rheum. 2007 Feb 15;57(1):6-12.

68. Hart DJ, Doyle DV, Spector TD. Incidence and risk factors for radiographic knee osteoarthritis in middle-aged women: the Chingford Study. Arthritis Rheum. 1999 Jan;42(1):17-24.

69. McAlindon TE, Wilson PW, Aliabadi P, Weissman B, Felson DT. Level of physical activity and the risk of radiographic and symptomatic knee osteoarthritis in the elderly: the Framingham study. Am.J.Med. 1999 Feb;106(2):151-7.

70. Manninen P, Heliovaara M, Riihimaki H, Suoma-Iainen O. Physical workload and the risk of severe knee osteoarthritis. Scand.J.Work Environ.Health 2002 Feb;28(1):25-32.

71. Rogers LQ, Macera CA, Hootman JM, Ainsworth BE, Blairi SN. The association between joint stress from physical activity and self-reported osteoarthritis: an analysis of the Cooper Clinic data. Osteoarthritis.Cartilage. 2002 Aug;10(8):617-22.

72. Fernandez WG, Yard EE, Comstock RD. Epidemiology of lower extremity injuries among U.S. high school athletes. Acad.Emerg.Med. 2007 Jul;14(7):641-5.

73. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. J.Athl.Train. 2007 Apr;42(2):311-9.

74. Vingard E, Alfredsson L, Malchau H. Osteoarthrosis of the hip in women and its relationship to physical load from sports activities. Am.J.Sports Med. 1998 Jan;26(1):78-82.

75. O'Connor MI. Sex differences in osteoarthritis of the hip and knee. J.Am.Acad.Orthop.Surg. 2007;15 Suppl 1:S22-S25.

76. Hootman JM, FitzGerald S.J., Macera CA, Blair S.N. Lower extremity muscle strength and risk of self-reported hip or knee osteoarthritis. J.Phys.Act.Health 2004;1(4):321-30.

77. Slemenda C, Heilman DK, Brandt KD, Katz BP, Mazzuca SA, Braunstein EM, Byrd D. Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women? Arthritis Rheum. 1998 Nov;41(11):1951-9.

78. Henry JC, Kaeding C. Neuromuscular differences between male and female athletes. Curr.Womens Health Rep. 2001 Dec;1(3):241-4.

79. Messier SP. Osteoarthritis of the knee and associated factors of age and obesity: effects on gait. Med.Sci.Sports Exerc. 1994 Dec;26(12):1446-52.

80. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. JAMA 2006 Apr 5;295(13):1549-55.

81. Prevalence of regular physical activity among adults--United States, 2001 and 2005. MMWR Morb.Mortal.Wkly.Rep. 2007 Nov 23;56(46):1209-12.

82. Cheng Y, Macera CA, Davis DR, Ainsworth BE, Troped PJ, Blair SN. Physical activity and self-reported, physician-diagnosed osteoarthritis: is physical activity a risk factor? J.Clin.Epidemiol. 2000 Mar 1;53(3):315-22.

83. Amin S, Guermazi A, Lavalley MP, Niu J, Clancy M, Hunter DJ, Grigoryan M, Felson DT. Complete anterior cruciate ligament tear and the risk for cartilage loss and

progression of symptoms in men and women with knee osteoarthritis. Osteoarthritis.Cartilage. 2008 Jan 17.

84. Deacon A, Bennell K, Kiss ZS, Crossley K, Brukner P. Osteoarthritis of the knee in retired, elite Australian Rules footballers. Med.J.Aust. 1997 Feb 17;166(4):187-90.

85. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. Am.J.Sports Med. 2007 Oct;35(10):1756-69.

86. Thelin N, Holmberg S, Thelin A. Knee injuries account for the sports-related increased risk of knee osteoarthritis. Scand.J.Med.Sci.Sports 2006 Oct;16(5):329-33.

87. Roos H, Lindberg H, Gardsell P, Lohmander LS, Wingstrand H. The prevalence of gonarthrosis and its relation to meniscectomy in former soccer players. Am.J.Sports Med. 1994 Mar;22(2):219-22.

88. Lane NE, Hochberg MC, Pressman A, Scott JC, Nevitt MC. Recreational physical activity and the risk of osteoarthritis of the hip in elderly women. J.Rheumatol. 1999 Apr;26(4):849-54.

89. Sutton AJ, Muir KR, Mockett S, Fentem P. A case-control study to investigate the relation between low and moderate levels of physical activity and osteoarthritis of the knee using data collected as part of the Allied Dunbar National Fitness Survey. Ann.Rheum.Dis. 2001 Aug;60(8):756-64.

90. Gordis L. Epidemiology. Philadelphia: W.B. Saunders; 1996.

91. Hootman JM, Macera CA, Helmick CG, Blair SN. Influence of physical activity-related joint stress on the risk of self-reported hip/knee osteoarthritis: a new method to quantify physical activity. Prev.Med. 2003 May;36(5):636-44.

92. Lievense AM, Bierma-Zeinstra SM, Verhagen AP, Bernsen RM, Verhaar JA, Koes BW. Influence of sporting activities on the development of osteoarthritis of the hip: a systematic review. Arthritis Rheum. 2003 Apr 15;49(2):228-36.

93. Vignon E, Valat JP, Rossignol M, Avouac B, Rozenberg S, Thoumie P, Avouac J, Nordin M, Hilliquin P. Osteoarthritis of the knee and hip and activity: a systematic international review and synthesis (OASIS). Joint Bone Spine 2006 Jul;73(4):442-55.

94. Exercise prescription for older adults with osteoarthritis pain: consensus practice recommendations. A supplement to the AGS Clinical Practice Guidelines on the management of chronic pain in older adults. J.Am.Geriatr.Soc. 2001 Jun;49(6):808-23.

95. Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation--United States, 2003-2005. MMWR Morb.Mortal.Wkly.Rep. 2006 Oct 13;55(40):1089-92.

96. Hootman JM, Helmick CG. Projections of US prevalence of arthritis and associated activity limitations. Arthritis Rheum. 2006 Jan;54(1):226-9.

97. Shih M, Hootman JM, Kruger J, Helmick CG. Physical activity in men and women with arthritis National Health Interview Survey, 2002. Am.J.Prev.Med. 2006 May;30(5):385-93.

98. Der Ananian CA, Wilcox S, Abbott J, Vrazel J, Ramsey C, Sharpe P, Brady T. The exercise experience in adults with arthritis: a qualitative approach. Am.J.Health Behav. 2006 Nov;30(6):731-44.

99. Der Ananian CA, Wilcox S, Saunders R, Watkins K, Evans A. Factors that influence exercise among adults with arthritis in three activity levels. Prev.Chronic.Dis. 2006 Jul;3(3):A81.

100. Wilcox S, Der AC, Abbott J, Vrazel J, Ramsey C, Sharpe PA, Brady T. Perceived exercise barriers, enablers, and benefits among exercising and nonexercising adults with arthritis: results from a qualitative study. Arthritis Rheum. 2006 Aug 15;55(4):616-27.

101. Fransen M, Nairn L, Winstanley J, Lam P, Edmonds J. Physical activity for osteoarthritis management: a randomized controlled clinical trial evaluating hydrotherapy or Tai Chi classes. Arthritis Rheum. 2007 Apr 15;57(3):407-14.

102. Schachter CL, Busch AJ, Peloso PM, Sheppard MS. Effects of short versus long bouts of aerobic exercise in sedentary women with fibromyalgia: a randomized controlled trial. Phys.Ther. 2003 Apr;83(4):340-58.

103. Ettinger WH, Jr., Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, Shumaker S, Berry MJ, O'Toole M, Monu J, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). JAMA 1997 Jan 1;277(1):25-31.

104. Mangani I, Cesari M, Kritchevsky SB, Maraldi C, Carter CS, Atkinson HH, Penninx BW, Marchionni N, Pahor M. Physical exercise and comorbidity. Results from the Fitness and Arthritis in Seniors Trial (FAST). Aging Clin.Exp.Res. 2006 Oct;18(5):374-80.

105. Penninx BW, Messier SP, Rejeski WJ, Williamson JD, DiBari M, Cavazzini C, Applegate WB, Pahor M. Physical exercise and the prevention of disability in

activities of daily living in older persons with osteoarthritis. Arch.Intern.Med. 2001 Oct 22;161(19):2309-16.

106. Hakkinen A, Sokka T, Kotaniemi A, Hannonen P. A randomized two-year study of the effects of dynamic strength training on muscle strength, disease activity, functional capacity, and bone mineral density in early rheumatoid arthritis. Arthritis Rheum. 2001 Mar;44(3):515-22.

107. Hakkinen A, Sokka T, Hannonen P. A home-based two-year strength training period in early rheumatoid arthritis led to good long-term compliance: a five-year followup. Arthritis Rheum. 2004 Feb 15;51(1):56-62.

108. Munneke M, de JZ, Zwinderman AH, Ronday HK, van SD, Dijkmans BA, Kroon HM, Vliet Vlieland TP, Hazes JM. Effect of a high-intensity weight-bearing exercise program on radiologic damage progression of the large joints in subgroups of patients with rheumatoid arthritis. Arthritis Rheum. 2005 Jun 15;53(3):410-7.

109. de Jong Z, Munneke M, Zwinderman AH, Kroon HM, Jansen A, Ronday KH, van SD, Dijkmans BA, Van den Ende CH, Breedveld FC, et al. Is a long-term high-intensity exercise program effective and safe in patients with rheumatoid arthritis? Results of a randomized controlled trial. Arthritis Rheum. 2003 Sep;48(9):2415-24.

110. Rejeski WJ, Focht BC, Messier SP, Morgan T, Pahor M, Penninx B. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. Health Psychol. 2002 Sep;21(5):419-26.

111. Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. JAMA 2001 Apr 18;285(15):1987-91.

112. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis.Cartilage. 2008 Feb;16(2):137-62.

113. Sullivan T, Allegrante JP, Peterson MG, Kovar PA, MacKenzie CR. One-year followup of patients with osteoarthritis of the knee who participated in a program of supervised fitness walking and supportive patient education. Arthritis Care Res. 1998 Aug;11(4):228-33.

114. Talbot LA, Gaines JM, Huynh TN, Metter EJ. A home-based pedometer-driven walking program to increase physical activity in older adults with osteoarthritis of the knee: a preliminary study. J.Am.Geriatr.Soc. 2003 Mar;51(3):387-92.

115. Wilkie R, Peat G, Thomas E, Croft P. Factors associated with restricted mobility outside the home in community-dwelling adults ages fifty years and older with knee pain: an example of use of the International Classification of Functioning to investigate participation restriction. Arthritis Rheum. 2007 Dec 15;57(8):1381-9.

116. Coleman EA, Buchner DM, Cress ME, Chan BK, de Lateur BJ. The relationship of joint symptoms with exercise performance in older adults. J.Am.Geriatr.Soc. 1996 Jan;44(1):14-21.

117. Ory M, Resnick B, Jordan PJ, Coday M, Riebe D, Ewing GC, Pruitt L, Bazzarre T. Screening, safety, and adverse events in physical activity interventions: collaborative experiences from the behavior change consortium. Ann.Behav.Med. 2005 Apr;29 Suppl:20-8.

118. Roddy E, Zhang W, Doherty M, Arden NK, Barlow J, Birrell F, Carr A, Chakravarty K, Dickson J, Hay E, et al. Evidence-based recommendations for the role of exercise in the management of osteoarthritis of the hip or knee--the MOVE consensus. Rheumatology.(Oxford) 2005 Jan;44(1):67-73.

119. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum. 2000 Sep;43(9):1905-15.

120. Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, Gunther K, Hauselmann H, Herrero-Beaumont G, Kaklamanis P, et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). Ann.Rheum.Dis. 2003 Dec;62(12):1145-55.

121. Zhang W, Doherty M, Arden N, Bannwarth B, Bijlsma J, Gunther KP, Hauselmann HJ, Herrero-Beaumont G, Jordan K, Kaklamanis P, et al. EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann.Rheum.Dis. 2005 May;64(5):669-81.

122. Bartels EM, Lund H, Hagen KB, Dagfinrud H, Christensen R, nneskiold-Samsoe B. Aquatic exercise for the treatment of knee and hip osteoarthritis. Cochrane.Database.Syst.Rev. 2007;(4):CD005523.

123. Brosseau L, MacLeay L, Robinson V, Wells G, Tugwell P. Intensity of exercise for the treatment of osteoarthritis. Cochrane.Database.Syst.Rev. 2003;(2):CD004259.

124. Busch AJ, Barber KA, Overend TJ, Peloso PM, Schachter CL. Exercise for treating fibromyalgia syndrome. Cochrane.Database.Syst.Rev. 2007;(4):CD003786.

125. Fransen M, McConnell S, Bell M. Exercise for osteoarthritis of the hip or knee. Cochrane.Database.Syst.Rev. 2003;(3):CD004286.

126. Jones KD, Adams D, Winters-Stone K, Burckhardt CS. A comprehensive review of 46 exercise treatment studies in fibromyalgia (1988-2005). Health Qual.Life Outcomes. 2006;4:67.

127. Lee MS, Pittler MH, Ernst E. Tai chi for rheumatoid arthritis: systematic review. Rheumatology.(Oxford) 2007 Nov;46(11):1648-51.

128. Lee MS, Pittler MH, Ernst E. Tai chi for osteoarthritis: a systematic review. Clin.Rheumatol. 2007 Sep 14.

129. Roddy E, Zhang W, Doherty M. Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. Ann.Rheum.Dis. 2005 Apr;64(4):544-8.

130. Van den Ende C, Vliet VT, Munneke M, Hazes J. Dynamic exercise therapy for treating rheumatoid arthritis. Cochrane.Database.Syst.Rev. 2000;(1):CD000322.

131. Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, Garry PJ, Lindeman RD. Epidemiology of sarcopenia among the elderly in New Mexico. Am.J.Epidemiol. 1998;147(8):755-63.

132. Visser M, Kritchevsky SB, Goodpaster BH, Newman AB, Nevitt M, Stamm E, Harris TB. Leg muscle mass and composition in relation to lower extremity performance in men and women aged 70 to 79: the health, aging and body composition study. J.Am.Geriatr.Soc. 2002;50(5):897-904.

133. Newman AB, Kupelian V, Visser M, Simonsick E, Goodpaster B, Nevitt M, Kritchevsky SB, Tylavsky FA, Rubin SM, Harris TB. Sarcopenia: alternative definitions and associations with lower extremity function. J.Am.Geriatr.Soc. 2003;51(11):1602-9.

134. Delmonico MJ, Harris TB, Lee JS, Visser M, Nevitt M, Kritchevsky SB, Tylavsky FA, Newman AB. Alternative definitions of sarcopenia, lower extremity performance, and functional impairment with aging in older men and women. J.Am.Geriatr.Soc. 2007;55(5):769-74.

135. Estrada M, Kleppinger A, Judge JO, Walsh SJ, Kuchel GA. Functional impact of relative versus absolute sarcopenia in healthy older women. J.Am.Geriatr.Soc. 2007;55(11):1712-9.

136. Janssen I. Influence of sarcopenia on the development of physical disability: the Cardiovascular Health Study. J.Am.Geriatr.Soc. 2006;54(1):56-62.

137. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J.Am.Geriatr.Soc. 2002;50(5):889-96.

138. Kirk EP, Washburn RA, Bailey BW, LeCheminant JD, Donnelly JE. Six months of supervised high-intensity low-volume resistance training improves strength independent of changes in muscle mass in young overweight men. J.Strength Cond.Res. 2007;21(1):151-6.

139. Sarsan A, Ardic F, Ozgen M, Topuz O, Sermez Y. The effects of aerobic and resistance exercises in obese women. Clin.Rehabil. 2006;20(9):773-82.

140. Pescatello LS, Kelsey BK, Price TB, Seip RL, Angelopoulos TJ, Clarkson PM, Gordon PM, Moyna NM, Visich PS, Zoeller RF, et al. The muscle strength and size response to upper arm, unilateral resistance training among adults who are overweight and obese. J.Strength Cond.Res. 2007;21(2):307-13.

141. Goodpaster BH, Park SW, Harris TB, Kritchevsky SB, Nevitt M, Schwartz AV, Simonsick EM, Tylavsky FA, Visser M, Newman AB. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. J.Gerontol.A.Biol.Sci.Med.Sci. 2006;61(10):1059-64.

142. Lord SR, Lloyd DG, Nirui M, Raymond J, Williams P, Stewart RA. The effect of exercise on gait patterns in older women: a randomized controlled trial. J.Gerontol.A.Biol.Sci.Med.Sci. 1996;51(2):M64-M70.

143. Lord SR, Ward JA, Williams P. Exercise effect on dynamic stability in older women: a randomized controlled trial. Arch.Phys.Med.Rehabil. 1996;77(3):232-6.

144. Cress ME, Buchner DM, Questad KA, Esselman PC, deLateur BJ, Schwartz RS. Exercise: effects on physical functional performance in independent older adults. J.Gerontol.A.Biol.Sci.Med.Sci. 1999;54(5):M242-M248.

145. Galvao DA, Taaffe DR. Resistance exercise dosage in older adults: single- versus multiset effects on physical performance and body composition. J.Am.Geriatr.Soc. 2005;53(12):2090-7.

146. Fahlman M, Morgan A, McNevin N, Topp R, Boardley D. Combination training and resistance training as effective interventions to improve functioning in elders. J.Aging.Phys.Act. 2007;15(2):195-205.

147. LaStayo PC, Ewy GA, Pierotti DD, Johns RK, Lindstedt S. The positive effects of negative work: increased muscle strength and decreased fall risk in a frail elderly population. J.Gerontol.A.Biol.Sci.Med.Sci. 2003;58(5):M419-M424.

148. Klentrou P, Slack J, Roy B, Ladouceur M. Effects of exercise training with weighted vests on bone turnover and isokinetic strength in postmenopausal women. J.Aging Phys.Act. 2007;15(3):287-99.

149. Taaffe DR, Pruitt L, Pyka G, Guido D, Marcus R. Comparative effects of high- and low-intensity resistance training on thigh muscle strength, fiber area, and tissue composition in elderly women. Clin.Physiol. 1996;16(4):381-92.

150. Adams KJ, Swank AM, Berning JM, Sevene-Adams PG, Barnard KL, Shimp-Bowerman J. Progressive strength training in sedentary, older African American women. Med.Sci.Sports Exerc. 2001;33(9):1567-76.

151. Kraemer WJ, Fleck SJ, Evans WJ. Strength and power training: physiological mechanisms of adaptation. Exerc.Sport Sci.Rev. 1996;24:363-97.

152. McCall GE, Byrnes WC, Dickinson A, Pattany PM, Fleck SJ. Muscle fiber hypertrophy, hyperplasia, and capillary density in college men after resistance training. J.Appl.Physiol. 1996;81(5):2004-12.

153. Harber MP, Fry AC, Rubin MR, Smith JC, Weiss LW. Skeletal muscle and hormonal adaptations to circuit weight training in untrained men. Scand.J.Med.Sci.Sports 2004;14(3):176-85.

154. Shaw I, Shaw BS. Consequence of resistance training on body composition and coronary artery disease risk. Cardiovasc.J.S.Afr. 2006;17(3):111-6.

155. Hisaeda H, Miyagawa K, Kuno S, Fukunaga T, Muraoka I. Influence of two different modes of resistance training in female subjects. Ergonomics 1996;39(6):842-52.

156. Staron RS, Karapondo DL, Kraemer WJ, Fry AC, Gordon SE, Falkel JE, Hagerman FC, Hikida RS. Skeletal muscle adaptations during early phase of heavy-resistance training in men and women. J.Appl.Physiol. 1994;76(3):1247-55.

157. Cureton KJ, Collins MA, Hill DW, McElhannon FM, Jr. Muscle hypertrophy in men and women. Med.Sci.Sports.Exerc. 1988;20(4):338-44.

158. Hostler D, Schwirian CI, Campos G, Toma K, Crill MT, Hagerman GR, Hagerman FC, Staron RS. Skeletal muscle adaptations in elastic resistance-trained young men and women. Eur.J.Appl.Physiol. 2001;86(2):112-8.

159. Eliakim A, Barstow TJ, Brasel JA, Ajie H, Lee WN, Renslo R, Berman N, Cooper DM. Effect of exercise training on energy expenditure, muscle volume, and maximal oxygen uptake in female adolescents. J.Pediatr. 1996;129(4):537-43.

160. Roth SM, Ivey FM, Martel GF, Lemmer JT, Hurlbut DE, Siegel EL, Metter EJ, Fleg JL, Fozard JL, Kostek MC, et al. Muscle size responses to strength training in young and older men and women. J.Am.Geriatr.Soc. 2001;49(11):1428-33.

161. Campos GE, Luecke TJ, Wendeln HK, Toma K, Hagerman FC, Murray TF, Ragg KE, Ratamess NA, Kraemer WJ, Staron RS. Muscular adaptations in response to three different resistance-training regimens: specificity of repetition maximum training zones. Eur.J.Appl.Physiol. 2002;88(1-2):50-60.

162. Ronnestad BR, Egeland W, Kvamme NH, Refsnes PE, Kadi F, Raastad T. Dissimilar effects of one- and three-set strength training on strength and muscle mass gains in upper and lower body in untrained subjects. J.Strength Cond.Res. 2007;21(1):157-63.

163. Candow DG, Burke DG. Effect of short-term equal-volume resistance training with different workout frequency on muscle mass and strength in untrained men and women. J.Strength Cond.Res. 2007;21(1):204-7.

164. Fielding RA. The role of progressive resistance training and nutrition in the preservation of lean body mass in the elderly. J.Am.Coll.Nutr. 1995 Dec;14(6):587-94.

165. Sipila S, Suominen H. Quantitative ultrasonography of muscle: detection of adaptations to training in elderly women. Arch.Phys.Med.Rehabil. 1996;77(11):1173-8.

166. Ferri A, Scaglioni G, Pousson M, Capodaglio P, Van Hoecke J, Narici MV. Strength and power changes of the human plantar flexors and knee extensors in response to resistance training in old age. Acta Physiol.Scand. 2003;177(1):69-78.

167. Suetta C, Aagaard P, Rosted A, Jakobsen AK, Duus B, Kjaer M, Magnusson SP. Training-induced changes in muscle CSA, muscle strength, EMG, and rate of force development in elderly subjects after long-term unilateral disuse. J.Appl.Physiol. 2004;97(5):1954-61.

168. Tsuzuku S, Kajioka T, Endo H, Abbott RD, Curb JD, Yano K. Favorable effects of non-instrumental resistance training on fat distribution and metabolic profiles in healthy elderly people. Eur.J.Appl.Physiol. 2007;99(5):549-55.

169. Klitgaard H, Mantoni M, Schiaffino S, Ausoni S, Gorza L, Laurent-Winter C, Schnohr P, Saltin B. Function, morphology and protein expression of ageing skeletal muscle: a cross-sectional study of elderly men with different training backgrounds. Acta Physiol Scand. 1990 Sep;140(1):41-54.

170. Fiatarone MA, Marks EC, Ryan ND, Meredith CN, Lipsitz LA, Evans WJ. High-intensity strength training in nonagenarians. Effects on skeletal muscle. JAMA 1990 Jun 13;263(22):3029-34.

171. Fiatarone MA, O'Neill EF, Ryan ND, Clements KM, Solares GR, Nelson ME, Roberts SB, Kehayias JJ, Lipsitz LA, Evans WJ. Exercise training and nutritional supplementation for physical frailty in very elderly people. N.Engl.J.Med. 1994 Jun 23;330(25):1769-75.

172. Binder EF, Yarasheski KE, Steger-May K, Sinacore DR, Brown M, Schechtman KB, Holloszy JO. Effects of progressive resistance training on body composition in frail older adults: results of a randomized, controlled trial. J.Gerontol.A.Biol.Sci.Med.Sci. 2005;60(11):1425-31.

173. Welle S, Totterman S, Thornton C. Effect of age on muscle hypertrophy induced by resistance training. J.Gerontol.A.Biol.Sci.Med.Sci. 1996;51(6):M270-M275.

174. Hakkinen K, Kallinen M, Izquierdo M, Jokelainen K, Lassila H, Malkia E, Kraemer WJ, Newton RU, Alen M. Changes in agonist-antagonist EMG, muscle CSA, and force during strength training in middle-aged and older people. J.Appl.Physiol 1998 Apr;84(4):1341-9.

175. Lemmer JT, Ivey FM, Ryan AS, Martel GF, Hurlbut DE, Metter JE, Fozard JL, Fleg JL, Hurley BF. Effect of strength training on resting metabolic rate and physical activity: age and gender comparisons. Med.Sci.Sports Exerc. 2001;33(4):532-41.

176. Dionne IJ, Melancon MO, Brochu M, Ades PA, Poelhman ET. Age-related differences in metabolic adaptations following resistance training in women. Exp.Gerontol. 2004;39(1):133-8.

177. Ivey FM, Roth SM, Ferrell RE, Tracy BL, Lemmer JT, Hurlbut DE, Martel GF, Siegel EL, Fozard JL, Jeffrey ME, et al. Effects of age, gender, and myostatin genotype on the hypertrophic response to heavy resistance strength training. J.Gerontol.A Biol.Sci.Med.Sci. 2000 Nov;55(11):M641-M648.

178. Hakkinen K, Kallinen M, Linnamo V, Pastinen UM, Newton RU, Kraemer WJ. Neuromuscular adaptations during bilateral versus unilateral strength training in middle-aged and elderly men and women. Acta Physiol Scand. 1996 Sep;158(1):77-88.

179. Wieser M, Haber P. The effects of systematic resistance training in the elderly. Int.J.Sports.Med. 2007;28(1):59-65.

180. Joseph LJ, Davey SL, Evans WJ, Campbell WW. Differential effect of resistance training on the body composition and lipoprotein-lipid profile in older men and women. Metabolism 1999;48(11):1474-80.

181. Bamman MM, Hill VJ, Adams GR, Haddad F, Wetzstein CJ, Gower BA, Ahmed A, Hunter GR. Gender differences in resistance-training-induced myofiber hypertrophy among older adults. J.Gerontol.A.Biol.Sci.Med.Sci. 2003;58(2):108-16.

182. Bishop D, Jenkins DG, Mackinnon LT, McEniery M, Carey MF. The effects of strength training on endurance performance and muscle characteristics. Med.Sci.Sports Exerc. 1999;31(6):886-91.

183. Korpelainen R, Keinanen-Kiukaanniemi S, Heikkinen J, Vaananen K, Korpelainen J. Effect of exercise on extraskeletal risk factors for hip fractures in elderly women with low BMD: a population-based randomized controlled trial. J.Bone Miner.Res. 2006 May;21(5):772-9.

184. Akima H, Takahashi H, Kuno SY, Masuda K, Masuda T, Shimojo H, Anno I, Itai Y, Katsuta S. Early phase adaptations of muscle use and strength to isokinetic training. Med.Sci.Sports Exerc. 1999;31(4):588-94.

185. Aagaard P, Simonsen EB, Trolle M, Bangsbo J, Klausen K. Specificity of training velocity and training load on gains in isokinetic knee joint strength. Acta Physiol.Scand. 1996;156(2):123-9.

186. DeMichele PL, Pollock ML, Graves JE, Foster DN, Carpenter D, Garzarella L, Brechue W, Fulton M. Isometric torso rotation strength: effect of training frequency on its development. Arch.Phys.Med.Rehabil. 1997;78(1):64-9.

187. Keeler LK, Finkelstein LH, Miller W, Fernhall B. Early-phase adaptations of traditional-speed vs. superslow resistance training on strength and aerobic capacity in sedentary individuals. J.Strength Cond.Res. 2001;15(3):309-14.

188. Putman CT, Xu X, Gillies E, MacLean IM, Bell GJ. Effects of strength, endurance and combined training on myosin heavy chain content and fibre-type distribution in humans. Eur.J.Appl.Physiol. 2004;92(4-5):376-84.

189. Hilliard-Robertson PC, Schneider SM, Bishop SL, Guilliams ME. Strength gains following different combined concentric and eccentric exercise regimens. Aviat.Space Environ.Med. 2003;74(4):342-7.

190. Mjolsnes R, Arnason A, Osthagen T, Raastad T, Bahr R. A 10-week randomized trial comparing eccentric vs. concentric hamstring strength training in well-trained soccer players. Scand.J.Med.Sci.Sports 2004;14(5):311-7.

191. Heitkamp HC, Horstmann T, Mayer F, Weller J, Dickhuth HH. Gain in strength and muscular balance after balance training. Int.J.Sports Med. 2001;22(4):285-90.

192. LaStayo PC, Pierotti DJ, Pifer J, Hoppeler H, Lindstedt SL. Eccentric ergometry: increases in locomotor muscle size and strength at low training intensities. Am.J.Physiol.Regul.Integr.Comp.Physiol. 2000;278(5):R1282-R1288.

193. Hass CJ, Garzarella L, de Hoyos DV, Connaughton DP, Pollock ML. Concurrent improvements in cardiorespiratory and muscle fitness in response to total body recumbent stepping in humans. Eur.J.Appl.Physiol. 2001;85(1-2):157-63.

194. Tsourlou T, Gerodimos V, Kellis E, Stavropoulos N, Kellis S. The effects of a calisthenics and a light strength training program on lower limb muscle strength and body composition in mature women. J.Strength.Cond.Res. 2003;17(3):590-8.

195. Dornemann TM, McMurray RG, Renner JB, Anderson JJ. Effects of high-intensity resistance exercise on bone mineral density and muscle strength of 40-50-year-old women. J.Sports.Med.Phys.Fitness. 1997;37(4):246-51.

196. Izquierdo M, Hakkinen K, Ibanez J, Kraemer WJ, Gorostiaga EM. Effects of combined resistance and cardiovascular training on strength, power, muscle cross-sectional area, and endurance markers in middle-aged men. Eur.J.Appl.Physiol. 2005;94(1-2):70-5.

197. King AC, Pruitt LA, Phillips W, Oka R, Rodenburg A, Haskell WL. Comparative effects of two physical activity programs on measured and perceived physical functioning and other health-related quality of life outcomes in older adults. J.Gerontol.A.Biol.Sci.Med.Sci. 2000;55(2):M74-M83.

198. Izquierdo M, Ibanez J, K HA, Kraemer WJ, Larrion JL, Gorostiaga EM. Once weekly combined resistance and cardiovascular training in healthy older men. Med.Sci.Sports.Exerc. 2004;36(3):435-43.

199. Tsourlou T, Benik A, Dipla K, Zafeiridis A, Kellis S. The effects of a twenty-four-week aquatic training program on muscular strength performance in healthy elderly women. J.Strength.Cond.Res. 2006;20(4):811-8.

200. Ballard JE, McFarland C, Wallace LS, Holiday DB, Roberson G. The effect of 15 weeks of exercise on balance, leg strength, and reduction in falls in 40 women aged 65 to 89 years. J.Am.Med.Womens Assoc. 2004;59(4):255-61.

201. Means KM, Rodell DE, O'Sullivan PS. Balance, mobility, and falls among community-dwelling elderly persons: effects of a rehabilitation exercise program. Am.J.Phys.Med.Rehabil. 2005;84(4):238-50.

202. de Vreede PL, Samson MM, van Meeteren NL, Duursma SA, Verhaar HJ. Functional-task exercise versus resistance strength exercise to improve daily function in older women: a randomized, controlled trial. J.Am.Geriatr.Soc. 2005;53(1):2-10.

203. Schlicht J, Camaione DN, Owen SV. Effect of intense strength training on standing balance, walking speed, and sit-to-stand performance in older adults. J.Gerontol.A.Biol.Sci.Med.Sci. 2001;56(5):M281-M286.

204. Asikainen TM, Suni JH, Pasanen ME, Oja P, Rinne MB, Miilunpalo SI, Nygard CH, Vuori IM. Effect of brisk walking in 1 or 2 daily bouts and moderate resistance training on lower-extremity muscle strength, balance, and walking performance in women who recently went through menopause: a randomized, controlled trial. Phys.Ther. 2006;86(7):912-23.

205. Topp R, Mikesky A, Dayhoff NE, Holt W. Effect of resistance training on strength, postural control, and gait velocity among older adults. Clin.Nurs.Res. 1996;5(4):407-27.

206. Latham NK, Bennett DA, Stretton CM, Anderson CS. Systematic review of progressive resistance strength training in older adults. J.Gerontol.A Biol.Sci.Med.Sci. 2004 Jan;59(1):48-61.

207. Francisco-Donoghue J, Werner W, Douris PC. Comparison of once-weekly and twice-weekly strength training in older adults. Br.J.Sports Med. 2007;41(1):19-22.

208. Rubenstein LZ, Josephson KR, Trueblood PR, Loy S, Harker JO, Pietruszka FM, Robbins AS. Effects of a group exercise program on strength, mobility, and falls among fall-prone elderly men. J.Gerontol.A.Biol.Sci.Med.Sci. 2000;55(6):M317-M321.

209. Haykowsky M, McGavock J, Vonder Muhll I, Koller M, Mandic S, Welsh R, Taylor D. Effect of exercise training on peak aerobic power, left ventricular morphology, and muscle strength in healthy older women. J.Gerontol.A.Biol.Sci.Med.Sci. 2005;60(3):307-11.

210. Engels HJ, Drouin J, Zhu W, Kazmierski JF. Effects of low-impact, moderate-intensity exercise training with and without wrist weights on functional capacities and mood states in older adults. Gerontology 1998;44(4):239-44.

211. Schnelle JF, MacRae PG, Giacobassi K, MacRae HS, Simmons SF, Ouslander JG. Exercise with physically restrained nursing home residents: maximizing benefits of restraint reduction. J.Am.Geriatr.Soc. 1996;44(5):507-12.

212. Sousa N, Sampaio J. Effects of progressive strength training on the performance of the Functional Reach Test and the Timed Get-Up-and-Go Test in an elderly population from the rural north of Portugal. Am.J.Hum.Biol. 2005;17(6):746-51.

213. Henwood TR, Taaffe DR. Short-term resistance training and the older adult: the effect of varied programmes for the enhancement of muscle strength and functional performance. Clin.Physiol.Funct.Imaging 2006;26(5):305-13.

214. Seynnes O, Fiatarone Singh MA, Hue O, Pras P, Legros P, Bernard PL. Physiological and functional responses to low-moderate versus high-intensity progressive resistance training in frail elders. J.Gerontol.A.Biol.Sci.Med.Sci. 2004;59(5):503-9.

215. Tsutsumi T, Don BM, Zaichkowsky LD, Delizonna LL. Physical fitness and psychological benefits of strength training in community dwelling older adults. Appl.Human Sci. 1997;16(6):257-66.

216. Bemben DA, Fetters NL, Bemben MG, Nabavi N, Koh ET. Musculoskeletal responses to high- and low-intensity resistance training in early postmenopausal women. Med.Sci.Sports Exerc. 2000 Nov;32(11):1949-57.

217. Hunter GR, Wetzstein CJ, McLafferty CL, Jr., Zuckerman PA, Landers KA, Bamman MM. High-resistance versus variable-resistance training in older adults. Med.Sci.Sports Exerc. 2001;33(10):1759-64.

218. Metter EJ, Conwit R, Tobin J, Fozard JL. Age-associated loss of power and strength in the upper extremities in women and men. J.Gerontol.A.Biol.Sci.Med.Sci. 1997;52(5):B267-B276.

219. Bean JF, Kiely DK, Herman S, Leveille SG, Mizer K, Frontera WR, Fielding RA. The relationship between leg power and physical performance in mobility-limited older people. J.Am.Geriatr.Soc. 2002;50(3):461-7.

220. Bean JF, Leveille SG, Kiely DK, Bandinelli S, Guralnik JM, Ferrucci L. A comparison of leg power and leg strength within the InCHIANTI study: which influences mobility more? J.Gerontol.A.Biol.Sci.Med.Sci. 2003;58(8):728-33.

221. Foldvari M, Clark M, Laviolette LC, Bernstein MA, Kaliton D, Castaneda C, Pu CT, Hausdorff JM, Fielding RA, Singh MA. Association of muscle power with functional status in community-dwelling elderly women. J.Gerontol.A.Biol.Sci.Med.Sci. 2000;55(4):M192-M199.

222. Suzuki T, Bean JF, Fielding RA. Muscle power of the ankle flexors predicts functional performance in community-dwelling older women. J.Am.Geriatr.Soc. 2001;49(9):1161-7.

223. Skelton DA, Young A, Greig CA, Malbut KE. Effects of resistance training on strength, power, and selected functional abilities of women aged 75 and older. J.Am.Geriatr.Soc. 1995 Oct;43(10):1081-7.

224. Jozsi AC, Campbell WW, Joseph L, Davey SL, Evans WJ. Changes in power with resistance training in older and younger men and women. J.Gerontol.A.Biol.Sci.Med.Sci. 1999;54(11):M591-M596.

225. Delmonico MJ, Kostek MC, Doldo NA, Hand BD, Bailey JA, Rabon-Stith KM, Conway JM, Carignan CR, Lang J, Hurley BF. Effects of moderate-velocity strength training on peak muscle power and movement velocity: do women respond differently than men? J.Appl.Physiol. 2005;99(5):1712-8.

226. Newton RU, Hakkinen K, Hakkinen A, McCormick M, Volek J, Kraemer WJ. Mixed-methods resistance training increases power and strength of young and older men. Med.Sci.Sports Exerc. 2002;34(8):1367-75.

227. Earles DR, Judge JO, Gunnarsson OT. Velocity training induces power-specific adaptations in highly functioning older adults. Arch.Phys.Med.Rehabil. 2001;82(7):872-8.

228. Fielding RA, LeBrasseur NK, Cuoco A, Bean J, Mizer K, Fiatarone Singh MA. High-velocity resistance training increases skeletal muscle peak power in older women. J.Am.Geriatr.Soc. 2002;50(4):655-62.

229. Signorile JF, Carmel MP, Czaja SJ, Asfour SS, Morgan RO, Khalil TM, Ma F, Roos BA. Differential increases in average isokinetic power by specific muscle groups of older women due to variations in training and testing. J.Gerontol.A.Biol.Sci.Med.Sci. 2002;57(10):M683-M690.

230. de Vos NJ, Singh NA, Ross DA, Stavrinos TM, Orr R, Fiatarone Singh MA. Optimal load for increasing muscle power during explosive resistance training in older adults. J.Gerontol.A.Biol.Sci.Med.Sci. 2005;60(5):638-47.

231. Surakka J, Aunola S, Nordblad T, Karppi SL, Alanen E. Feasibility of power-type strength training for middle aged men and women: self perception, musculoskeletal symptoms, and injury rates. Br.J.Sports Med. 2003;37(2):131-6.

232. Bean J, Herman S, Kiely DK, Callahan D, Mizer K, Frontera WR, Fielding RA. Weighted stair climbing in mobility-limited older people: a pilot study. J.Am.Geriatr.Soc. 2002;50(4):663-70.

233. Bean JF, Herman S, Kiely DK, Frey IC, Leveille SG, Fielding RA, Frontera WR. Increased velocity exercise specific to task (InVEST) training: a pilot study exploring

effects on leg power, balance, and mobility in community-dwelling older women. J.Am.Geriatr.Soc. 2004;52(5):799-804.

234. Sayers SP, Bean J, Cuoco A, LeBrasseur NK, Jette A, Fielding RA. Changes in function and disability after resistance training: does velocity matter? A pilot study. Am.J.Phys.Med.Rehabil. 2003;82(8):605-13.

235. Miszko TA, Cress ME, Slade JM, Covey CJ, Agrawal SK, Doerr CE. Effect of strength and power training on physical function in community-dwelling older adults. J.Gerontol.A.Biol.Sci.Med.Sci. 2003;58(2):171-5.

236. Orr R, de Vos NJ, Singh NA, Ross DA, Stavrinos TM, Fiatarone-Singh MA. Power training improves balance in healthy older adults. J.Gerontol.A.Biol.Sci.Med.Sci. 2006;61(1):78-85.

237. Bottaro M, Machado SN, Nogueira W, Scales R, Veloso J. Effect of high versus low-velocity resistance training on muscular fitness and functional performance in older men. Eur.J.Appl.Physiol. 2007;99(3):257-64.