

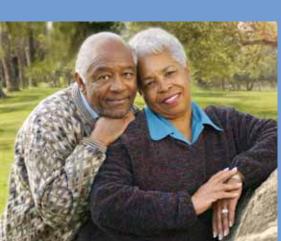
Living Long & Well in the 21st Century Strategic Directions for Research on Aging



U.S. Department of Health and Human Services







NIA Director's Message

We are pleased to share through this document our best insights into the future of research on aging and the role of the National Institute on Aging (NIA) in realizing that future. These broad strategic goals and objectives have been identified through discussions among NIA staff members with input from the National Advisory Council on Aging, NIA's Board of Scientific Counselors, and other representatives of the research and advocacy communities.

As we look to the future, we foresee unprecedented opportunities brought about by advances in science and technology coupled with the challenge of using our best scientific judgment to make difficult choices, in some cases, about which areas of research to pursue. Our NIA intramural and extramural scientists work alongside our grantees and partners in other Institutes and Centers at the National Institutes of Health (NIH), other government agencies, and the private sector to build synergy and leverage resources to help make it possible for older adults to experience healthier, more productive lives. We strive to gain a clearer understanding of what we term "normal" aging along with deeper insights into a multitude of diseases and conditions with increased risk and severity among older adults. And we use that knowledge to develop and test more effective interventions that will indeed allow people to live long and well in the 21st century.

We hope that readers will find the information in this document a useful resource for facilitating and advancing dialogue about research on aging.

Richard J. Hodes, M.D.

Director, National Institute on Aging

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November 2007



This Document Online

This document is available online at **www.nia.nih.gov/AboutNIA/StrategicDirections**. The online version includes hyperlinks to information about NIA programs and initiatives associated with the various priority areas described in this document.

Other Helpful Web Sites:

National Institute on Aging Home Page – www.nia.nih.gov

Current Funding Opportunities for Research and Training – www.nia.nih.gov/GrantsAndTraining

NIA Extramural Research Programs - www.nia.nih.gov/ResearchInformation/ExtramuralPrograms

Biology of Aging Program - www.nia.nih.gov/bap

Behavioral and Social Research Program - www.nia.nih.gov/bsr

Neuroscience and Neuropsychology of Aging Program - www.nia.nih.gov/nna

Geriatrics and Clinical Gerontology Program – www.nia.nih.gov/gcg

NIA Intramural Research Programs - www.grc.nia.nih.gov

National Institutes of Health Home Page - www.nih.gov

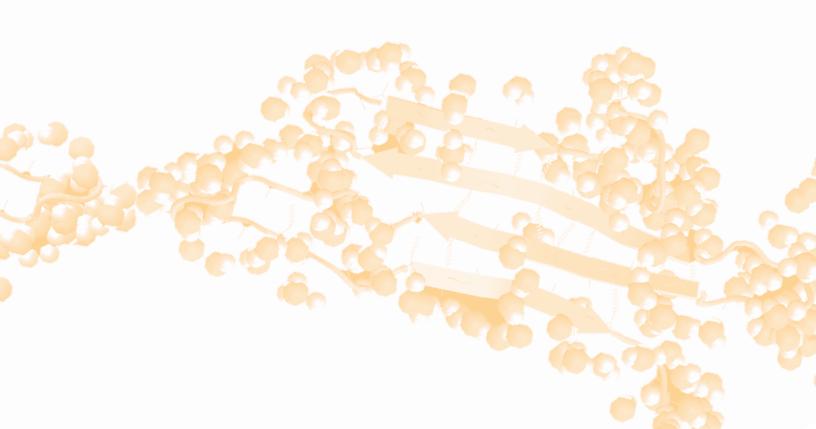
NIH Roadmap for Medical Research - nihroadmap.nih.gov

NIH Blueprint for Neuroscience Research – neuroscienceblueprint.nih.gov



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Introduction

The face of aging in the United States is changing dramatically. People are living longer, achieving higher levels of education, living in poverty less often, and experiencing increasingly lower rates of disability. Life expectancy nearly doubled during the 20th century with a ten-fold increase in the number of Americans age 65 or older. Today, there are approximately 35 million Americans age 65 or older, and this number is expected to double in the next 25 years. The oldest old people age 85 or older—constitute the fastest growing segment of the U.S. population. Currently about four million people, this population could top 19 million by 2050. And living to 100 is becoming increasingly commonplace. In 1950, there were approximately 3,000 American centenarians. By 2050, there could be nearly one million. The challenge for the 21st century will be to make these added years as healthy and productive as possible and to continue the current trend of decline in disability across all segments of the population.

Modern medicine and new insights into lifestyle and other environmental influences are allowing a growing number of people to remain healthy and socially and emotionally vital into advanced ages. As life expectancy increases, however, diseases and conditions that threaten the health of older people remain a concern. For example, more than half of all Americans 65 or older show evidence of osteoarthritis in at least one joint. One in every two women and one in four men over age 50 will break a bone due to osteoporosis. Alzheimer's disease (AD), cardiovascular disease, cancer, and diabetes remain widespread among older Americans. In addition, many older Americans suffer from multiple health problems, and the existence of such comorbidities often complicates treatment and can dramatically affect quality of life.

Our ability to reduce the burden of illness among older adults will depend on an increased understanding of the dynamics of aging and how they interact with various environmental and lifestyle factors in individuals. We need to explore "aging" not as a single process but rather as an intricate web of interdependent genetic, biochemical, physiological, economic, social, and psychological factors, some of which are better understood than others. In addition to research on the biological basis of aging, some scientists are working to gain new insights into disease processes and comorbidities, the prevalence of which increases with advanced age, and to use this knowledge to develop more effective ways to prevent, diagnose, and treat diseases and conditions of aging. Others are exploring behavioral and social factors involved in aging and how they interact with genetics and biology. Still others are concerned with the economic and societal consequences of a rapidly aging population. Building on past discoveries, we will continue to focus on finding effective interventions to ensure that as people live longer, they can do so in better health and with greater independence.

The National Institute on Aging

The National Institute on Aging leads a national scientific effort to understand the nature of aging in order to promote the health and well-being of older adults. NIA is one of the 27 Institutes and Centers that make up the National Institutes of Health, a component of the U.S. Department of Health and Human Services.

NIA Research Focuses on the Increased Risk and Severity of Health Problems As People Age

Older adults are healthier than ever today, but the risk and severity of a number of diseases and conditions increase with age. Much of NIA-supported research focuses on uncovering the molecular and cellular determinants of disease risk as well as the changes that occur with age at the organ, tissue, cellular, and molecular levels that may lead to dysfunction. Some investigators examine age-related processes from multiple perspectives, including those of the genetic, biological, clinical, behavioral, social, and economic sciences. Other studies focus on specific diseases or conditions with increased prevalence as people age. Many of the disease-specific research projects we support are collaborative efforts with other Institutes at the NIH.

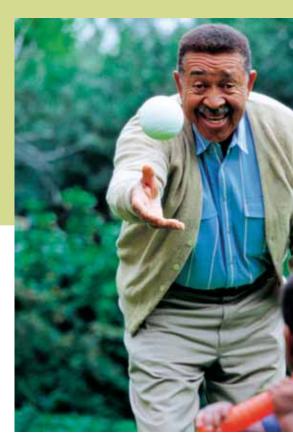
- With increasingly sophisticated technological tools, we hope someday to unravel the mysteries that still surround Alzheimer's disease, changes in memory and cognition, and other degenerative diseases of the nervous system, and to develop interventions to prevent, diagnose early, and treat these conditions.
- Exciting developments in our understanding of cardiovascular disease,

cancer, and diabetes interface with new findings about the basic processes of aging and may soon open doors for personalized approaches to preempt, prevent, or treat these diseases across the lifespan.

- Better options for helping older adults with vision, hearing, and other sensory disorders will dramatically improve the quality of life for these individuals.
- For people who suffer from bone, muscle, skin, joint, and movement disorders, new insights about nutrition and exercise, better surgical options, better understanding of the basic biology leading to new therapies, and more user-friendly assistive technology hold promise for helping them lead more comfortable and active lives.
- Ongoing developments hold promise for finding better ways to help health care providers and caregivers more effectively address a variety of ageassociated disorders such as frailty, falls, delirium, incontinence, sleep disturbances, and depression.
- Researchers are also gaining new insights into the psychological, psychiatric, and social changes that

occur with age—from studies of the psychological adaptation to aging and disease to the development of strategies to address the behavioral symptoms of dementia or stress.

NIA-supported research also focuses on the effects of chronic illness and the comorbidities that are so common among older adults. For example, NIA researchers are studying the demonstrated association between certain cardiovascular disorders such as atherosclerosis (hardening of the arteries) and hyperlipidemia (elevated blood levels of certain types of fat) and the risk for neurological disease and other agerelated disorders. Others are investigating the relationship between metabolic disorders such as diabetes and cognitive decline in older adults.



The Institute's mission is to:

- Support and conduct genetic, biological, clinical, behavioral, social, and economic research related to the aging process, diseases and conditions associated with aging, and other special problems and needs of older Americans.
- Foster the development of research and clinician scientists in aging.
- Communicate information about aging and advances in research on aging to the scientific community, health care providers, and the public.

We carry out our mission by supporting extramural research at universities and medical centers across the United States and around the world and a vibrant intramural research program at NIA laboratories in Baltimore and Bethesda, Maryland.

This document outlines the broad strategic directions of the Institute and provides a point of reference for setting priorities and a framework for systematically analyzing the Institute's scientific portfolio and assessing progress in achieving our



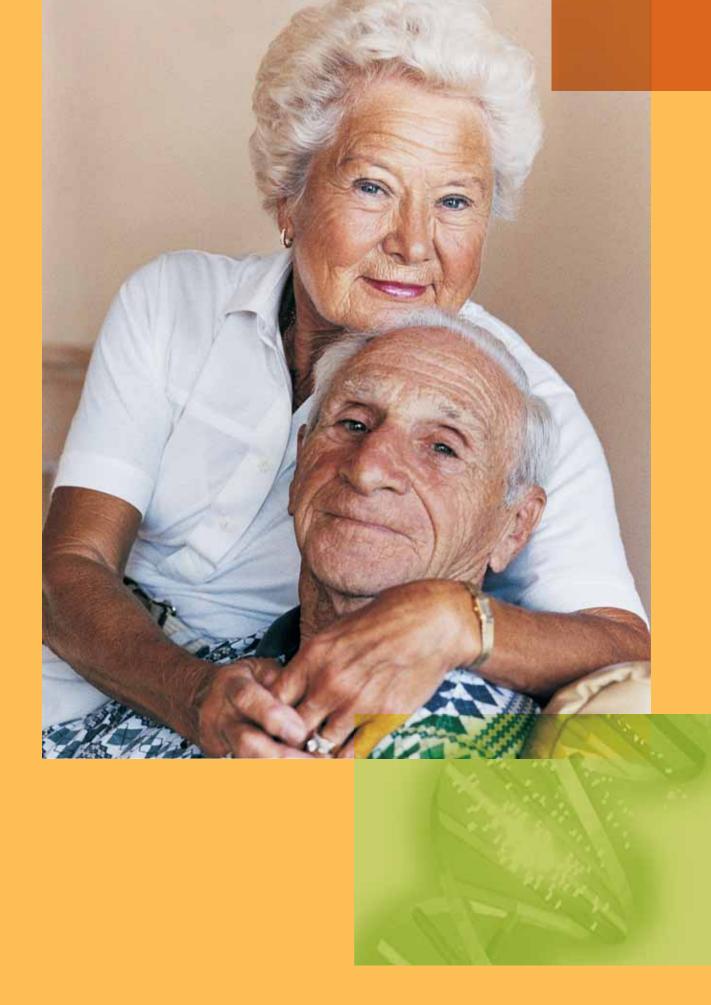
mission. NIA strives to ensure that funding decisions and research initiatives address current and projected public health needs and take full advantage of scientific and technological opportunities for advancing the field of research on aging. With constant monitoring of the health needs of our older population and regular consultation with our stakeholders, we will optimize our efforts to improve the quality of life of older adults.

Our goals are to:

- A Improve our understanding of healthy aging and disease and disability among older adults.
- **B** Continue to develop and disseminate information about interventions to reduce disease and disability and improve the health and quality of life of older adults.
- C Improve our understanding of Alzheimer's disease, other dementias of aging, and the aging brain. Develop drug and behavioral interventions for treating these diseases, preventing their onset and progression, and maintaining cognitive, emotional, sensory, and motor health.
- **D** Improve our understanding of the consequences of an aging society and provide that information to inform intervention development and policy decisions.
- **E** Improve our ability to reduce health disparities and eliminate health inequities among older adults.
- Support the infrastructure and resources needed to promote high-quality research and communicate its results.

Our vision is to:

Achieve a time when people in their "golden years" enjoy robust health and independence, remain physically active, and continue to make positive contributions to their families and communities.



Research Goal A

Improve our understanding of healthy aging and disease and disability among older adults.

ging comprises a set of dynamic biological, physiological, and psychosocial processes and systems—interactive and independent—that result in wide variations among individuals. Adult aging often involves common changes that may not be harmful such as graying hair. For many, however, aging also means a progressive and inexorable loss of function leading to increased vulnerability to disease, frailty, and disability. Many hypotheses and theories to explain this decline have been offered through the years, but none by itself can explain the array of physical, biological, and psychological changes that take place as people age.

NIA-supported researchers are beginning to define the link between genes and lifespan. For example, numerous genes have been implicated in normal aging processes, in age-related pathologies and diseases, and in the longevity of several species including humans. Researchers are also identifying the interactions among genes; the environment; and lifestyle, behavioral, and social factors and their influence on the initiation and progression of some diseases. Further research is needed to determine the roles and interaction of these diverse factors in aging.

One of our challenges in this research is to develop a clearer understanding of the normal changes that accompany aging and distinguish them from the diseases and disabilities that are prevalent among older adults. A common thread, for example, is the process of inflammation, which leads over time to changes in cell, tissue, and organ structure and function. Inflammation may increase the susceptibility

to and rate of progression of age-related pathologies and may contribute to frailty, independent of overt disease. This and other risk or protective processes that may occur at various stages, from early life on, may influence health and survival outcomes in old age. Many older people also suffer from anemia, thrombosis, involuntary weight loss, dizziness, sensory deficits such as hearing or vision loss, dementia, frailty, or incontinence. Research into the underlying causes of these and other geriatric syndromes is needed in order to develop new prevention strategies and treatment approaches.

NIA-supported research is also helping to identify lifestyle factors and health behaviors that directly influence physical, cognitive, and emotional fitness and risk of disease. Scientists are developing and refining recommendations for people of all ages regarding optimal diet, use of dietary supplements, mental stimulation, physical exercise, quality sleep, and other healthy practices to increase their likelihood of enjoying healthy old age. Still other researchers are looking for better ways to enhance the physical, mental, and interpersonal abilities of older people and to expand opportunities for them to achieve personal goals and contribute to society in meaningful ways. As we identify more precisely these behaviors and lifestyles that influence health and quality of life, we will be able to reinforce prevention efforts, enhance symptom management, conserve function, and improve caregiving.

To more fully understand aging processes and their relationship to disease and disability among older people, NIA will:

- **A-1** Support studies on healthy aging, well-being, and longevity.
- **A-2** Accelerate the discovery of the causes and risk factors associated with disease and disability among older adults.
- **A-3** Encourage translational research to bridge basic discovery and intervention development.

A-1 Support studies on healthy aging, well-being, and longevity.

Research on the biology of aging has revolutionized our understanding of healthy aging. New findings about genetic, molecular, and cellular factors and processes that affect the course of aging are providing valuable insights about aging, longevity, and the genesis of disease. Similarly, population studies are uncovering potential risk factors such as environmental exposures, health-related behaviors, and social factors, as well as the influence of co-existing conditions across the lifespan and their relationship to the progression of disease. NIA will continue research to:

- Identify cellular and molecular factors that determine the pace of aging processes.

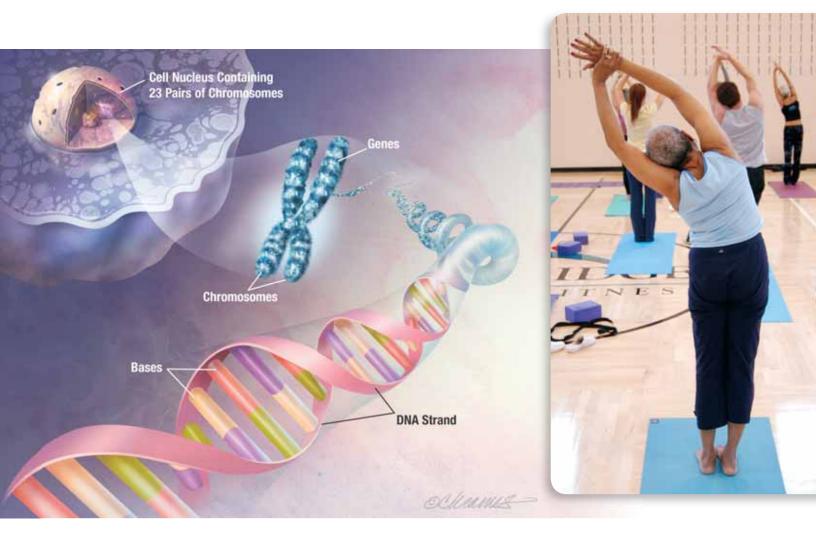
 Researchers have identified key factors affecting the pace of aging, including the body's response to a variety of stresses, the function of the immune system, and the role of cellular senescence (deterioration of the cell) as a tumor suppression mechanism. NIA will work to identify additional factors and to elucidate the role of each of these processes in the aging human.
- Determine how the cellular and molecular bases of changes associated with aging contribute to decreased function and increased incidence of disease. Although increasing age is most often accompanied by a significant and progressive

Our Genes Are Key to How We Age

The way we age depends on a mixture of intrinsic and extrinsic forces. Extrinsic factors such as healthy habits can be controlled. However, a significant portion of aging is determined by genes, which may encode causative factors involved in aging or factors that delay aging and/or promote extended health span (longevity assurance factors). In humans, it has been estimated that genetics control 25 to 40 percent of life and health span variability, but the identity of the responsible genes is difficult to pinpoint. Basic researchers have identified about 100 genes that control lifespan in model organisms, including roundworms called nematodes, yeast, fruit flies, and mice. Further research is needed to understand the relationships among these genes and to determine whether or not the equivalent genes in humans function in a similar fashion. Research has also identified subtle and reversible changes in human genes, which, in some cases, can be passed from generation to generation and can control the level of activity of some genes. These "epigenetic" changes represent another area of research that might yield further insights into aging and age-related disease.

Scientists supported by NIA are particularly interested in identifying genetic factors that contribute to healthy aging as well as unraveling the genetic and biological processes involved in age-related traits and diseases. Our hope is that the discovery and increased understanding of genes involved in aging and longevity will lead to the development of medical and behavioral interventions that can slow the aging process and, most importantly, delay or prevent the onset of age-associated diseases.

decline in almost all physiological functions, resulting in increased susceptibility to age-related chronic diseases, some functions are remarkably well maintained in a large number of people. NIA will encourage research in both the loss and maintenance of functions during the aging process. Many researchers suspect that this increase in susceptibility to diseases may be due to the changes occurring as a result of the aging process itself. Therefore, manipulation of the basic



processes of aging might provide an effective way to prevent or treat age-related diseases. We will foster comprehensive studies both in humans and in animal models to investigate the health- and disease-related effects of manipulating the process of aging at the molecular level.

Identify developmental, prenatal, early life, and environmental processes that affect aging, age changes, and disease. Harmful substances can exert profound physical effects on a developing fetus, while childhood exposure to environmental agents such as infections or drugs can greatly limit adult physical and cognitive health and longevity. NIA will continue to support epidemiological studies to identify such factors and participate in translational studies to find ways to minimize their effects in adults.

Understand the role of stem cells in tissue maintenance and how stem cells and their environments change with age. Stem cells contribute to tissue development and replenishment throughout life. Stem cells are the ultimate precursors to all the cells of the body, and they are important tools for both cell-based therapies and regenerative medicine. It is clear that tissues and organs lose function with advanced age, and such losses may result from declines in stem cell function. This loss of function occurs at different levels, including the stem cells themselves, the microenvironment where they self renew and differentiate (the niche), the receptiveness of the target tissues, or even in the communication among the target tissues, the niches, and the stem cells. NIA will pursue the major challenges in cell-based therapies and regenerative medicine, including improvement of the mobilization of native

stem cell pools and definition of the limitations of stem cell expansion ex vivo, so that stem cells can be grown in adequate numbers for tissue repair while preserving their potency. NIA will also foster research to create a detailed molecular and functional understanding of stem cells, their niches, and their target microenvironments as well as strategies to direct stem cell differentiation into specific cell types. This research will inform efforts to understand and alter the aged environments that decrease stem cell function and improve the efficiency with which stem cells reach their target sites, where they can be effective while minimizing potentially harmful side effects.

- Understand the influence of obesity and metabolic status in healthy aging. We will continue collaborative studies on the relationships among obesity, insulin signaling, hypertension, and diabetes. We will continue studies on the efficacy of various nutritional and other cognitive and behavioral approaches to maintaining a healthy weight and preventing cardiovascular disease, cancer, diabetes, neurodegenerative disease, musculoskeletal conditions, and other conditions in older people. This research will also help determine whether or not general recommendations for healthy eating, physical exercise, and sleep in the young or middle aged are optimal for older people.
- Understand the sensory and motor changes associated with aging and how they lead to decreased function and increased incidence of disease. Mobility changes in the aging adult can be age related or the precursor to more severe motor disorders. Loss of sensory functions such as vision, hearing, or the ability to taste foods may result from aging-related processes or may be an indication of more severe underlying diseases or conditions. We will promote a better understanding of the underlying mechanisms of these



and other age-associated changes. This research will provide the knowledge base necessary to develop interventions that optimize mobility and sensory function and prevent disease in the later years of life.

Continue to support basic research in the psychological science of aging. Understanding agerelated psychological change remains essential for advancing our understanding of how age impacts behaviors and decisions that, in turn, shape the subjective well-being, social relationships, physical and mental health, physical function, and economic well-being of older adults. Advances in psychological science are needed to improve behavioral interventions, and to understand the pathways and mechanisms through which psychological and social factors impact health. NIA continues to support research on basic psychological and social processes associated with normal aging; their relationship to individual, contextual, and environmental factors that impact these outcomes; and their neurobiological and genetic basis.



- Continue research on the impact of social interaction on health and well-being. Although research suggests that positive social interaction is health protective, we must improve our understanding of the mechanisms and pathways through which these factors improve both physical and mental health. We must also better identify the characteristics of social relationships and social environments that promote healthy aging. NIA-supported research to deepen our understanding in this area will aid in tailoring interventions to improve the health and quality of life of older adults.
- Explore the interplay between genetic, biological, clinical, social, economic, psychological, and environmental factors affecting aging and longevity. Evidence suggests that these factors and their interplay are critical to minimizing disease and achieving full potential and vitality in later years. More research is needed to verify the linkages and to better understand their underlying mechanisms.

- Identify factors across the lifespan that contribute to exceptional health or its decline. The study of older people is shedding light on the biological, behavioral, and social factors associated with healthy aging. We will continue research that links laboratory and longitudinal populationbased studies, providing insights into the factors that define resilient individuals and contribute to well-being in old age.
- Expand our knowledge of age- and longevityassociated genes as well as epigenetic alterations that affect longevity and well-being, including modes of action. NIA-supported research has shown that patterns of extreme longevity run in families. Furthermore, scientists have identified approximately 100 different genes that affect longevity in model organisms. We will continue work to identify the biological functions of longevity genes and to better understand the mechanisms of action of known and yet-to-beidentified longevity genes (longevity assurance genes). This research will facilitate the development of biologically-based interventions to promote longevity, delay age-related dysfunction, extend health span, and improve the quality of life of older people.

Epigenetic alterations (modifications other than changes in the DNA sequence that alter gene expression) are also likely to play important roles in rates of aging, age-related dysfunctions, and development of age-related diseases. Like changes to the DNA sequence itself, epigenetic modifications can be inherited. These modifications affect the cellular machinery responsible for turning genes "on" or "off," allowing or preventing them from functioning optimally. Environmental agents such as chemicals or dietary components can also modify DNA and can be transmitted to offspring.

- Refine our understanding of the interplay among the biological, social, emotional, cognitive, and functional changes associated with normal aging. The impact of changes in emotional, cognitive, and physical capacities at different life stages—in combination with life course changes in motivation and goals—on social and economic behaviors at different life stages remains unknown. We know even less about changes in the neurobiological underpinnings of these interactions. NIA will use the approaches of social neuroscience and neuroeconomics to study how the neurobiological changes associated with aging influence or are influenced by social, emotional, cognitive, and motivational factors.
- Elucidate the biological mechanisms and pathways through which social, psychological, and environmental stresses contribute to declines in health and well-being among older adults. Individual differences in the subjective experience and physiological and psychological impact of stressors may exacerbate or buffer the impact of stressors on health. We will encourage multi-level and interdisciplinary research in collaboration with relevant NIH Institutes on the interactive effects of genes, behavior, and social environments on health and well-being as people age.

A-2 Accelerate the discovery of the causes and risk factors associated with disease and disability among older adults.

To develop new interventions for the prevention, early detection and diagnosis, and treatment of aging-related diseases, disorders, and disabilities, we must first understand their causes and the factors that place people at increased risk for their initiation and progression. NIA will continue research to:



- Identify the genetic and epigenetic bases of agerelated diseases and conditions as well as factors that affect disease initiation and progression. Studies of genes associated with aging processes, longevity, and age-related diseases will continue to provide insights into disease pathologies and vulnerability. However, emerging research suggests that epigenetic mechanisms may also underlie, in part, the susceptibility to common and complex diseases of aging, particularly those subject to environmental influences. We will support research to understand the basic mechanisms influencing the aging process as a whole. In addition, we will work to understand the interplay among genes and environmental influences, as this knowledge will be essential to our understanding of the development of both disease and healthy aging.
- Improve our understanding of the molecular, genetic, cellular, and tissue bases of aging that contribute to increased risk for, alter the course of, and vary the response to the treatment of major age-associated diseases. We will increase efforts to understand the genetic and epigenetic factors that can alter susceptibility of individuals to disease and affect the response to treatment. In addition, we will work in collaboration with other NIH Institutes and Centers to study how phenomena such as anxiety and other negative

Inflammation Plays an Important Role in the Aging Process

Inflammation is a natural and highly regulated response that provides protection and promotes healing when infection or injury occurs. However, if left unregulated, these same processes can cause further tissue injury and damage. It is unclear to what extent acute or chronic inflammation influences the pace of aging. Also unknown is whether age-related changes in inflammatory responses reflect a "normal" deterioration of cells or are the result of disease processes, or if psychological factors such as stress could promote the development of chronic inflammation or exacerbate its effects.

Inflammatory processes, particularly those resulting in chronic inflammation, have been implicated in a number of chronic diseases and conditions of aging, including cardiovascular disease, osteoarthritis, osteoporosis, Alzheimer's disease, insulin resistance and diabetes, muscle wasting, and frailty. However, the precise role of inflammation in each of these conditions is not well understood. NIAsupported researchers are working to describe more fully the underlying biology connecting the mediators of inflammation with these disease processes, including:

- How inflammatory mediators—molecules that coordinate the inflammatory response at the cellular level—change with age, and how these changes contribute to disease
- How "normal" age-related cellular changes may trigger an inflammatory response
- How chronic or acute inflammation resulting from disease or dysfunction contributes to-or protects against-further cellular dysfunction

Ultimately, NIA-supported investigators hope to apply an improved understanding of inflammatory processes and their cellular mechanisms to develop more precisely targeted anti-inflammatory interventions.

- emotions can alter nervous system function. Although these processes aid the body in responding to dangerous or stressful situations, they can damage cells, tissues, and organ systems when produced in excess.
- Identify the molecular and cellular bases of agerelated decline in immune responses. The agerelated decrease in the adaptive immune response (that is, the cellular response for manufacturing antibodies and killing pathogens) makes older people more prone to a variety of infectious agents and reduces the efficacy of vaccinations in older adults. These factors have a significant effect on the health span and quality of life of older people. We will support research to develop more protective vaccine regimens and strategies to improve immune responses in the aging population.
- Improve our understanding of how the inflammatory process is affected by aging and how these changes impact tissue function. The degree to which primary age-related changes in inflammation contribute to changes in structure and function of various tissues and organs as well as the risk or progression of age-related pathologies and conditions is not clear. Likewise, researchers are continuing to identify the sources of proinflammatory cytokines (proteins used by the body for cell-to-cell communication). We will examine the role of different cell types, including immune cells and adipose tissue (fat), in the age-related increase in levels of pro-inflammatory cytokines. We will also investigate how changes in the circulating levels of these cytokines contribute to pathological changes in tissues and organs. We will facilitate exploration of how the response of different tissues to pro-inflammatory cytokines is affected by age and how these changes contribute to the overall balance of the immune system.



■ Identify, analyze, and track changing patterns of disability for older adults and better understand factors contributing to these patterns. The current pattern of increased "active life expectancy," the average number of years an individual will live without a limiting disease or disability in parallel with increased length of life, is threatened by increases in obesity and disability rates for younger cohorts. NIA-supported research will address disability dynamics at several levels, including longitudinal research to understand the determinants of onset, severity, and recovery from disabling conditions. At the population level, we will foster research to understand the pathways to disability and the causes of change in mobility and function over time as well as subgroup disparities. We will also invest in research on more sensitive measures of functional disability that are needed to better track these changes.

A-3 Encourage translational research to bridge basic discovery and intervention development.

Translational research provides the two-way bridge necessary to link scientific discoveries with applications in medical practice and public health. For research on aging, basic discoveries typically begin with studies at a molecular or cellular level to understand the mechanisms of normal aging and disease or with studies to better understand the basic behavioral and social science related to aging processes. New knowledge gained at "the bench" takes a variety of paths to human intervention studies—the "bedside." Equally important is providing a clear path back to the bench for insights gained at the bedside. Several NIH initiatives are focusing on the broad issues of culture change required for the biomedical community to more successfully support translational activities. In support of our other objectives in Research Goal A, NIA will continue to:

The Quest for Biomarkers Takes Many Pathways

A biomarker is a physical, biochemical, or functional measure used as an indicator of a physiological change or disease process. Biomarkerssometimes referred to as surrogate markers or clinical endpoints-can be used to define, diagnose, or predict disease and enable rational treatment and monitoring of disease. Basic mechanistic studies of specific disorders can identify molecules in biological fluids, tissues, or even breath with which disease-related changes could be identified as disease biomarkers. Biomarker imaging tools such as positron emission tomography (PET), magnetic resonance imaging (MRI), and nuclear magnetic resonance (NMR) spectroscopy scans can reveal detailed alterations in tissue due to disease processes and permit noninvasive longitudinal tracking of disease progression. Other biomarkers help determine cognitive declines

through standardized neuropsychological test batteries or the effect of environmental triggers or social stress factors on aging and health outcomes. Some biomarkers can also predict susceptibility to disease or serve as measures of drug toxicity.

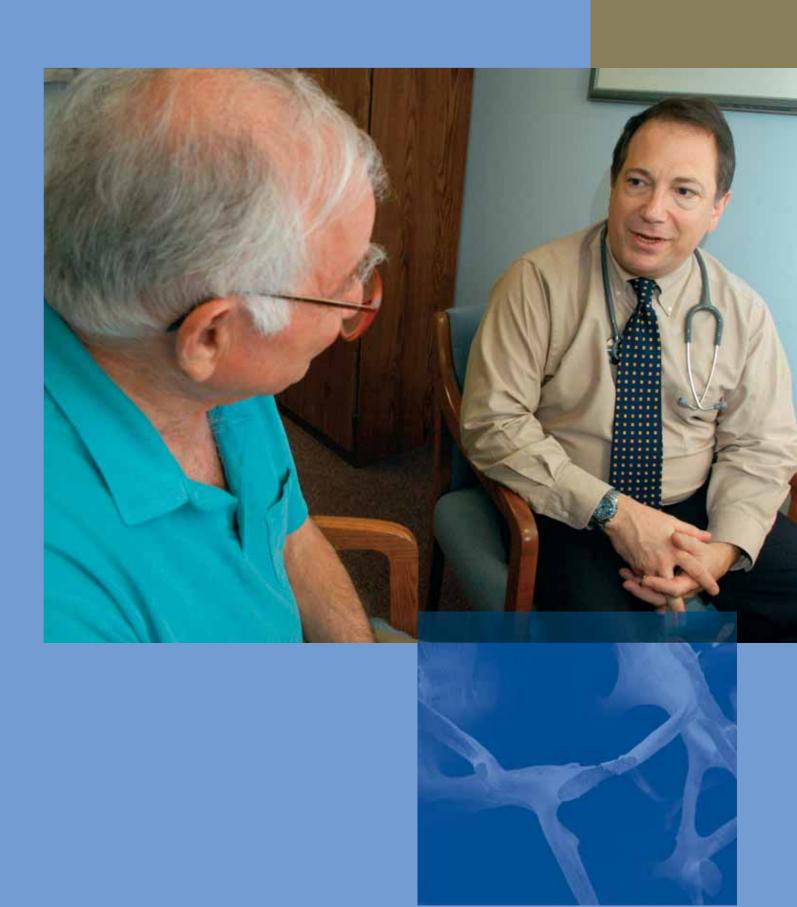
There is a critical lack of specific, reliable, quantifiable, and easily measured biomarkers that correlate well with early disease progression. Public and private organizations have invested heavily in identifying candidate disease biomarkers using technologies such as imaging, genomics, proteomics, and high-throughput approaches. NIA-supported initiatives help to refine technologies for biomarker discovery and apply them to specific diseases. The Alzheimer's Disease Neuroimaging Initiative, for example, seeks to identify whether longitudinal and concurrent brain imaging and biochemical measure-

ments can be used to monitor disease progression. Improved brain imaging promises to provide researchers with the ability to monitor how drugs affect the accumulation of harmful proteins as disease progresses. Biological samples from well-characterized patients enrolled in this and similar studies are made available for other investigations.

NIA is working to improve the precision and validity of biomarkers for monitoring the progression of other diseases such as osteoarthritis or assessing an individual's risk of cardiovascular disease or diabetes. Advanced biomarker technology also promises to streamline clinical trials by identifying clinical subtypes to establish more homogeneous study populations and applying biomarker testing to monitor and assess the effects of trial interventions.

- Identify and optimize opportunities for moving new knowledge from basic discovery to intervention development and back. We will accelerate our efforts to promote promising preclinical studies and health systems research. We will also work to ensure that new technologies such as advanced imaging and bioinformatics and other resources needed for effective translational research are accessible to NIA-supported scientists and clinicians.
- Facilitate communication among NIA-supported researchers and encourage interdisciplinary collaboration. The complexity of contemporary science demands a synergistic approach to ensure collaboration among researchers from multiple scientific disciplines along the continuum of research. We will invest in multidisciplinary research programs

- and provide supplemental funding to support promising interdisciplinary endeavors.
- Foster communication and partnerships with other NIH Institutes and Centers and with other Federal agencies as well as other national and international research organizations. NIA will continue to collaborate with other NIH Institutes and Centers on projects with a multidisciplinary focus such as the NIH Roadmap for Medical Research and the NIH Blueprint for Neuroscience Research. We will continue to participate in partnerships with outside organizations to share resources, support collaborative research, eliminate barriers to drug development, and communicate research findings to the public.



Research Goal B

Continue to develop and disseminate information about interventions to reduce disease and disability and improve the health and quality of life of older adults.

odern medicine and new insights into lifestyle and other environmental influences promise to have a profound impact on the health and well-being of older people and make it possible for them to remain physically healthy and cognitively and emotionally vital into very advanced ages ideally, for as long as they live. Capitalizing on new insights from basic research, NIA-supported scientists, often in collaboration with other NIH Institutes and Centers, will continue to work from multiple perspectives to develop and test strategies for preempting or reducing the severity of the full range of health problems experienced by older people. We will work to strengthen the translation of basic findings in the laboratory into practical applications to improve the health and quality of life of older adults.

Our success will depend on progress in achieving three objectives in this area:

- **B-1** Develop effective interventions to maintain health and function and prevent or reduce the burden of age-related diseases, disorders, and disabilities.
- **B-2** Understand and develop strategies to enhance societal roles and interpersonal support for older adults, reduce social isolation, and prevent elder abuse.
- **B-3** Increase awareness and promote adoption of interventions to improve the health and quality of life of older people.

B-1 Develop effective interventions to maintain health and function and prevent or reduce the burden of age-related diseases, disorders, and disabilities.

Achieving and maintaining health and function in advanced years can be aided by physical fitness, proper nutrition, and avoidance of smoking and other behaviors that adversely affect health. Conversely, unhealthy lifestyle choices may be associated with significant health problems. However, research has shown that it is almost never too late to decrease risk of disease and disability by establishing healthier patterns. Improved health habits can help people survive longer, enable them to postpone the onset of disability, and increase quality of life and function at older ages. Research has also shown that optimizing both the physical and social environment is important to the health and functioning of older people.

NIA will continue to:

 Develop efficacious and cost-effective strategies for promoting and ensuring adherence to healthy and safe behaviors among older adults.

- Build on our understanding of the roles of nutrition, obesity, sleep, and metabolic status to develop more effective health maintenance strategies. Epidemiological studies—and, in some cases, studies in animals—have shown clear positive effects of manipulations such as dietary restriction and negative effects of obesity, malnutrition, and less-than-optimal sleep patterns on health and age-related morbidity. We will use these and other findings to develop and test in clinical trials cost-effective dietary and other behavioral measures and adherence strategies for the prevention or delay of disease and disability.
- Use our increased understanding of exercise physiology and other branches of basic science to maximize the positive effect of exercise on older people. Several studies strongly suggest that modest exercise may have beneficial effects in maintaining health—including mental health—and that these benefits are possible even at advanced ages. For example, weight-bearing exercise can build bone strength, consequently preventing osteoporosis and subsequent fragility fractures. We will support further research to validate exercise and exercise programs and their effects on older people within specific age groups and develop strategies for promoting adherence.
- Continue research to understand hormone changes in older people and pursue the development of interventions to address these changes without unwanted side effects. Counteracting some effects of aging by supplementing hormones such as estrogen, testosterone, human growth hormone, melatonin, and DHEA (dehydroepiandrosterone) is an area of active study, but there are concerns that individuals may be taking such agents before their safety and efficacy

- have been established. We support studies to understand the biological action of hormonal changes in older men and women, assess whether or not hormone therapy will improve health, investigate the use of compounds to produce the beneficial responses of hormones in the body without detrimental side effects, and determine the potential to regulate hormone production in specific body tissues where increased or decreased amounts of these hormones are favorable to health.
- Develop strategies to reduce falls and their consequences. NIA-supported human factors research will continue to identify safety risks for older people in home and work environments, improve screening strategies, and develop and disseminate information important to reducing the risk of falls.
- Explore new ways to improve safety in the home and community through studies of ergonomics and the built environment. We will continue to support research to identify cost-effective alterations in design that can reduce injuries and provide a safer, more secure environment for older adults.
- Pursue a better understanding of needs and develop interventions to improve the safety of older drivers. We will continue research to identify factors such as visual impairment, hearing, attention, speed of processing, and other cognitive changes that put older drivers at risk of automobile accidents. In addition, we will continue to support the development of tools for assessing visual, cognitive, and other abilities associated with safe driving, interventions to improve the physical and cognitive skills necessary for safe driving, and technology to support the special needs of older drivers. We will also support research to understand the dynamics of making the decision to stop driving, the implications of that decision for the health and well-being of older people, and alternative transportation options that help older adults maintain as much independence as possible.

- This research will provide the insights needed to develop guidelines for older adults, their health care providers, and family members.
- Improve the safe use of medications by older adults. Managing medications can be complex for older people, many of whom take drugs, often prescribed by more than one physician, for multiple health problems. Complications include adverse drug interactions and interactions with dietary supplements coupled with the physiological and functional changes associated with aging or age-related diseases. NIA-supported research will improve our understanding and maximize the effectiveness of medications, develop new technical aids for physicians to monitor drug use, and provide new technologies and information to enable patients to manage medications better and avoid adverse reactions.
- Develop interventions for treating, preventing, or delaying the onset of age-related diseases and conditions.
 - Support research into the mechanisms by which lifestyle interventions affect aging-related changes and determine how individuals can maintain function with age or regain that function after loss due to immobility, illness, or trauma. After peaking in early adulthood, most tissue functions decline with advancing age. This leads to increased risks for developing diseases such as cardiovascular disease and cancer, and may lead to declines in overall health and quality of life. Further research is needed on the mechanisms through which common interventions, both medical and behavioral, may slow physical and cognitive decline. NIA will continue to support research into the mechanisms of functional decline and its delay, with the goals of identifying molecular targets for drug interventions and treatments that minimize losses and promote the recovery of function after illness or trauma.

- Test compounds that hold the promise of increasing healthy lifespan. Promising compounds must undergo preclinical safety and efficacy testing using animal and cellular models before being tested in full-scale clinical trials. We will continue to support the testing of promising compounds in mice and other model systems with the long-term goal of selecting for further development those most likely to have a beneficial effect in humans.
- Conduct clinical studies and encourage the translation of new interventions to the clinical setting. As pathways and processes of disease are better defined, basic research findings can be translated expeditiously to the development of clinical applications. We will continue to support clinical studies to improve health and well-being through better treatments for agerelated diseases and conditions and to test the effects of hormone therapy, dietary supplementation, and exercise and fitness. We will work with others to facilitate the navigation of barriers to the translation of promising compounds into clinical trials and ultimately approval by the U.S. Food and Drug Administration.

- Develop improved approaches for the early detection and diagnosis of disabling illnesses and age-related debilitating conditions. We will help develop and evaluate improved techniques and tools to measure the well-being of older people as well as symptoms of disease and disability. As new interventions are ready, we will facilitate the movement of biochemical, imaging, and other technologies into mainstream medical practice, where they can be used routinely to assist in early detection and diagnosis as well as to monitor the efficacy of interventions tested in clinical trials.
- Find significantly improved and cost-effective ways to reduce caregiver, family, and patient stress and improve older people's ability to cope with chronic disease. Families and others who care for people with chronic disease frequently face emotional stress as well as physical and financial burdens. Investigators will continue to evaluate strategies to improve social support, skills training, and assistive services both for those who cope with chronic disease and for their caregivers. NIA-supported research will clarify needs and patterns of family caregiving and how people make decisions on providing care and inform guidance on support and skills, including a focus on families with diverse ethnic and socioeconomic backgrounds.
- Develop strategies to improve the interaction of older people with the health system. For older adults and their families, effective health care requires quality communication with and among health care professionals. According to one study, fewer than 40 percent of people experiencing symptoms associated with heart and circulatory or musculoskeletal systems seek a physician's care. Similarly, women often avoid seeking care for urinary incontinence. NIA will help develop strategies to assist patients in dealing with multiple

services and to manage health care financing for multiple chronic conditions. We will seek better interventions to help older people recognize the implications of disease-related signs and symptoms and consult a physician or other health care provider when they first occur. And we will work to find ways to help health care providers coordinate their services to older adults.

B-2 Understand and develop strategies to enhance societal roles and interpersonal support for older adults, reduce social isolation, and prevent elder abuse.

Despite negative stereotypes, millions of older people work productively and otherwise contribute to society and place a high value on retaining their independence. Research suggests that social support and continued involvement in useful activities foster positive effects both on physical and mental health and on longevity. This effort is especially important for older adults who are at increased risk for multiple diseases, disability, and functional limitations that may keep them from fully engaging in the world around them. Improvements in acute and long-term health care for older people are also essential, including strategies to ease the burdens of caregivers and enhance quality of care at home and in different long-term care settings. These initiatives should result in more effective approaches for prevention, treatment, and rehabilitation.

NIA will continue to:

■ Identify ways for older people to retain valued roles and maintain independence. Older men and women are now working in paid jobs, doing essential volunteer work, maintaining a household, and/or supporting children and grandchildren. NIA-supported research will seek and apply technological, social, and behavioral findings to extend the ability of older adults to remain independent, active, and productive.



- Conduct research on the social and economic aspects of family caregiving and develop and disseminate effective interventions for patient care in family and community settings. Intergenerational family support is the most common way in which a family assembles and allocates its resources of money, skills, and time to care for all its members.
 - Assess and evaluate family relationships over time. This research will help us understand the effects of changing relationships on the health and well-being of older people, and gain insight into the caregiving, emotional support, and family-level economic aspects of aging.
 - Address issues centered on the increased demands faced by family caregivers in light of changing patterns of work and family demographics. We will pay particular attention to the ways in which characteristics such as gender, marital status, income, socioeconomic status, race, and ethnicity influence these demands.
- Develop strategies to help older people and their families prepare for and manage age-associated changes in health, income, function, and roles. Older adults and family members are faced with many complex decisions about retirement, finances, health and life insurance, and medical treatment. Issues of concern include the ability of health care delivery systems to support patient and family needs and adherence to a patient's advanced directives. NIA-supported research will inform decisions about complex issues of health, finances, and family roles in late life, both for individuals and policymakers. We will compile up-to-date information about patterns of work and retirement, sources of retirement income, intergenerational income transfers, and status of health and disability at the regional, national, and global levels. This compilation will be used to develop and make available information and other resources for people as they plan for later life transitions and possible loss of independence as well as to inform policy decisions.

- Research and develop strategies to improve decision making for long-term and end-of-life care. There is a pressing need to define organizational mechanisms that will ensure quality, affordable health care for older people. There is also a critical lack of empirically generated knowledge on how to maximize quality at the end of life. Medical culture is oriented primarily to patient care and not to addressing the multifaceted needs of dying patients and their families. To better address these issues, we will:
 - Examine component parts of health care delivery systems and their impact on medical, social, functional, and cost outcomes and use this information to develop interventions to improve care.

 This research will help inform the development of interventions to coordinate care that promotes attention to patient and family preferences, facilitates smooth transitions among care settings, and maximizes independence. We will explore ways to support long-term care, most often provided in a home setting. We will focus on interventions that reduce the burdens of caregivers, with an emphasis on the unique challenges faced by patients with dementia and their caregivers.
 - Understand caregiving patterns and improve the effectiveness of different strategies for helping families manage the care needs of the physically frail. For example, we will use knowledge gained from this research to develop and disseminate evidence-based guidance on caregiving skills, environmental modifications, and technological supports for both informal and formal longterm care settings.
 - Develop strategies to improve the experience of older people at the end of life. We will support research to better understand the decision-making process and changing preferences associated with advance care planning; better understand the transitions among end-of-life care settings such as the home, hospital, nursing home, and hospice; assess the benefit of end-

Dissemination of Research Results Is a Critical Component of the NIA Mission

An essential component of the NIA mission is the dissemination of information about research and aging-related topics to the general public, health professionals, the media, policymakers, and advocacy organizations. The Institute reaches out to the public through the NIA Web site, two Information Clearinghouses with toll-free numbers, and the NIHSeniorHealth Web site.

- The NIA Web site, www.nia.nih.gov, offers information about NIA programs, research findings, grants and training opportunities, and public and professional education materials. The NIA Spanish-language Web site, www.nia. nih.gov/Espanol has information on a wide range of health topics, free publications in Spanish, and links to other health-related, Spanish-language Web sites.
- The NIA Information Center, 1-800-222-2225, distributes a variety of public and professional education materials, including Age Pages on more than 40 health topics from arthritis and diabetes to sleep and skin care. NIA's evidence-based Exercise Guide provides simple, easy-tofollow exercises to improve endurance, strength, flexibility, and balance.
- The Alzheimer's Disease Education and Referral (ADEAR)
 Center, 1-800-438-4380, offers information on diagnosis, treatment, patient care, caregiver needs, clinical trials, and research related to Alzheimer's disease.
- www.NIHSeniorHealth.gov is a collaborative effort with the National Library of Medicine. Based on research on cognition and aging, the site provides information on more than 30 health topics. Information is available in a variety of senior-friendly formats, including large print, opencaption videos, and audio versions.

of-life therapies and the cost effectiveness of interventions to improve end-of-life care; develop better measures of end-of-life quality for the patient and the family to improve our understanding of psychosocial issues that impact the end-of-life experience; and understand the social and economic context of caring for an older person who is dying.

- Assess the impact of health care organizations and provider interactions on the quality of life for dying individuals. Special attention will be given to developing strategies that enhance support of the older person, the family, and medical care providers who are attempting to provide humane and life-affirming services at the end of life.
- Understand and develop strategies to address elder neglect and abuse. Although isolated studies have documented the devastating long-term consequences of elder mistreatment, research on elder neglect and abuse has been inadequate. We will support methodological research to help determine the prevalence of elder physical, psychological, and financial neglect and abuse. We will also work to develop and disseminate reliable measurement tools for assessing neglect and abuse and interventions to reduce its incidence.

B-3 Increase awareness and promote adoption of interventions to improve the health and quality of life of older people.

Communication efforts play a critical role in educating the public about research advances to improve health and well-being in later life. Health communication activities can increase the public's awareness of a specific aging issue, problem, or solution; reinforce certain knowledge, attitudes, or health behaviors; dispel misconceptions about aging; and encourage individual or collective action. Health education programs, activities, and materials also can inform, influence, and motivate the public.

Communicating effectively about health is challenging. Health information is often complex and technical. Moreover, the information may be inconclusive, controversial, contradictory, or subject to change as new research findings are released. Health information also may conflict with long held personal beliefs. To succeed, health communication programs and materials must be based on an appreciation of the needs and interests of the target audience. Large scale, multi-year, multi-media efforts

utilizing community organizations already in place may be needed to inform, persuade, convince, and sustain behavior change. To address these concerns and ensure that research results are disseminated to all who need them, NIA will:

- Develop, test, and conduct health communication programs and outreach activities to inform the public about the interventions and health-related progress validated by the results of research on aging. We will craft and deliver messages and materials based on research to understand how the target audience perceives and reacts to health messages, how the public is persuaded to change behavior, and how people in general, and older people in particular, respond to various media.
- Develop appropriate materials and programs for a variety of target audiences. We will continue to work to overcome gender, cultural, and language barriers to the effective communication of health information.
- Explore successful networks for the transfer of research knowledge and evaluate the usefulness of transferred interventions for older adults in broadly designed and applied outcomes research. NIA will continue to work with other Federal agencies, State and local governments, and the private and nonprofit sectors to ensure that results of research on behavioral and community interventions are widely shared and have an impact on policies and programs.
- Provide information to support the training of people who work with older adults. We will provide professional societies, community organizations, and academic institutions with research-based information that can be used in training geriatricians, social workers, counselors, and other community professionals and volunteers to work effectively with older adults and to implement evidence-based interventions.



Research Goal C

Improve our understanding of Alzheimer's disease, other dementias of aging, and the aging brain. Develop drug and behavioral interventions for treating these diseases, preventing their onset and progression, and maintaining cognitive, emotional, sensory, and motor health.

better understanding of how the brain ages will provide important information on which to base strategies for maintaining and enhancing cognitive, emotional, sensory, and motor function through biological and behavioral interventions. For example, studies have shown that new neurons form in certain regions of the brain even in adulthood. This phenomenon, known as neurogenesis, suggests that medical and behavioral approaches could be found to stimulate the formation of new neurons to compensate for the loss and functional decline of neurons with aging, disease, or traumatic injury. NIA will support research to harness functional imaging and other advanced technologies that view activity in specific regions of the brain to identify age-related neural changes and mechanisms the older brain uses to maintain optimal learning, memory, and other cognitive functions. We will also work to clarify the interactions between the brain and the peripheral nervous, endocrine, hematopoietic, cardiovascular, and immune systems. We will also support the development of preventive and therapeutic approaches to maintaining health in cognition, emotion, sleep function, sensory processes, and motor function. Research on the function of the normal brain and peripheral nervous system will help us understand the ways in which non-dementia-related health outcomes arise.

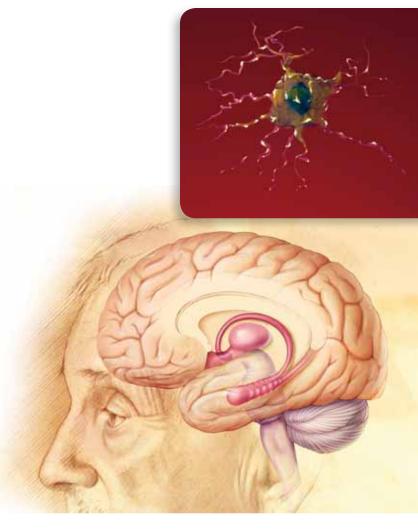
Our objectives in this area are to:

- C-1 Understand the mechanisms involved in normal brain aging; the role of cognition in everyday functioning; protective factors for sensory, motor, emotional, and cognitive function; and the pathogenesis of AD and other neurodegenerative disorders of aging.
- C-2 Develop better ways of distinguishing people with normal brain aging from those who will develop mild cognitive impairment (MCI), AD, and related conditions.
- C-3 Translate discoveries about the cellular and molecular mechanisms of cognitive, emotional, sensory, and motor function with age and the mechanisms of AD pathogenesis into diagnostic, treatment, and/or prevention strategies.
- C-4 Conduct research to better understand and develop interventions to address the special caregiving needs of patients with AD and other dementias.

C-1 Understand the mechanisms involved in normal brain aging; the role of cognition in everyday functioning; protective factors for sensory, motor, emotional, and cognitive function; and the pathogenesis of AD and other neurodegenerative disorders of aging.

NIA will continue research to:

■ Improve our understanding of nervous system and behavioral changes that occur with normal aging and how brain function is maintained and enhanced. Changes in brain structure and function, some of which may compensate for age-related decrements, may continue throughout life. For example, research shows that the hippocampus, a region of the brain important for acquiring and processing information, is capable of generating new nerve cells. Furthermore, research in mice demonstrates that increased physical and mental activity started in middle age can increase hippocampal neurogenesis and decrease signs of neuronal aging. This suggests that neurogenesis may be one factor underlying the beneficial effects of an active lifestyle on brain integrity and behavioral function in humans. We will continue to explore the role of physical and mental exercise in promoting healthy cognitive, emotional, and motor functioning and in activating the cellular machineries that protect the brain from damage and promote its repair. This research will help form the basis for future investigation of more subtle neural changes that occur with age, including selective neuronal loss or dysfunction that impacts memory and other functions, impaired neuronal connections, early brain atrophy, and changes in the responses of glial cells involved in neuron survival and brain plasticity and possibly inflammation.



■ Determine how genetic, molecular, cellular, and environmental factors interact for optimal brain health and functioning, including in the oldest old. The overall integrity of brain structure and many neural systems are largely preserved in normal aging, while in age-related diseases, specific brain cell types and their connections are damaged or lost. Evidence suggests that achieving the full potential of the central and peripheral nervous systems depends on developing the brain optimally in early life, continuing activity to maintain function in midlife, and stimulating the brain to compensate for cell death

We Need To Better Distinguish **Patterns of Brain Aging**

As with other bodily organ systems, brain function declines with age. Many older people notice changes in memory, learning, or other cognitive performance. These changes are associated with loss of neurons, the basic operative cells of the brain. The extent of "normal" brain aging varies among individuals and can be somewhat difficult to quantify. With "abnormal" brain aging, however, cognitive losses are typically more severe, and after the individual dies, significant pathological changes related to underlying disease processes are usually found in the brain at autopsy. The early identification of people at risk for abnormal brain aging is the subject of intense ongoing research on genetic, biochemical, and neuropsychological aspects of the transition from normal to pathologic aging.

Standardized neuropsychological tests have been developed and validated with consensus thresholds of abnormal performance that aid clinicians in evaluating mild cognitive impairment and dementia. The development of drug therapies or behavioral modifications to slow or possibly halt the complex processes involved in cognitive decline requires the earliest possible intervention. Hence researchers are searching for biochemical or imaging markers that might be used to predict the clinical course of dementia versus normal aging patterns or to monitor treatment progress. A better understanding of factors involved in normal and abnormal brain aging will aid our ability to enhance healthy brain aging, for example with dietary and behavioral practices that could prolong normal brain function.

and injury in older age. We will work to gain a greater understanding of the many factors that interact to maintain brain function, including compensatory mechanisms and adaptive or dynamic changes. This research will enhance our understanding of, and potentially our ability to prevent, brain function decline in aging and disease.

For example, we will:

- Continue to pursue a greater understanding of the interaction among genetic factors that underlie normal cognitive, emotional, sensory, and motor function as well as abnormal decline and the interactions between genetics and the environment.
- Investigate epigenetic changes, which can significantly influence the structure and function of genes within the cell.
- Support research to better understand the neurological and behavioral effects of environmental factors, both early and later in life.

In addition, we will continue to investigate the changes in brain function that take place in the oldest old, people 85 or older. In the absence of disease, many of these individuals continue to lead healthy and productive lives even into unusually old age. Others, however, suffer from health conditions that can contribute to cognitive decline and dementia, emotional dysfunction, motor instability, and/or sensory deficits. We will work to identify and address the conditions that most affect brain health in this group in order to find ways to maintain function as long as possible.

■ Understand the role of cognition in everyday functioning, including work environments, decision making, and interaction with technology. NIA will support research to examine the influence of contexts—behavioral, social, cultural, and technological—on the cognitive functioning of older adults; investigate the effects of agerelated changes in cognition on activities of daily living, social relationships, and health status; and develop strategies for improving everyday functioning through various interventions such as cognitive training.

- Explore possible additional risk and protective factors for brain health and function, cognitive decline, mild cognitive impairment, and AD through epidemiological and other population studies. Community-based studies of aging and AD are becoming progressively more sophisticated. Traditional interviews, clinical evaluations, and routine laboratory tests are increasingly complemented by advanced imaging and other technologies to identify risk factors and protective factors and to relate them to specific biological mechanisms. NIA will place a special emphasis on community-based studies, including studies in racial and ethnic minority populations, capable of linking early life or midlife factors with late life cognitive decline or impairment. We will include studies of the ways that multiple factors such as lifestyle, genetics, comorbid diseases, or sensory or motor dysfunction interact to cause disease or contribute to cognitive decline.
- Refine our knowledge of molecular, cellular, cognitive, and other behavioral changes that cause or accompany development of AD and other dementias of aging. We will investigate the multiple pathological changes associated with the development of AD, including accumulation of abnormal proteins, loss of synapses, and death of neurons. We will promote further characterization of these pathological changes in tissue culture, animal models, and humans. Our research will also address the behavioral and psychological changes associated with the development of AD as well as psychiatric conditions such as clinical depression. This research will enhance our basic knowledge of altered neural, cognitive, and behavioral function in older adults and will aid in the development of appropriate treatments.



■ Investigate the relationship between systemic metabolism and brain function during normal aging and in AD. Epidemiological research has shown that the presence of metabolic and vascular risk factors such as obesity, diabetes, hypertension, and heart disease during midlife as well as current smoking are associated with accelerated age-related cognitive decline and with increased risk for AD. This association is even more pronounced in individuals with three or more vascular risk factors. Given the prevalence of obesity and other components of metabolic syndrome in the U.S. population, we will stimulate research to examine the mechanisms by which disrupted systemic metabolism may influence the transition between normal brain aging and AD. This effort will provide not only a better understanding of the etiology of AD, but may also benefit the search for biomarkers of cognitive aging and AD. Ultimately we are interested in exploring whether the negative impact of metabolic and vascular risk factors on brain aging can be counteracted through behavioral and lifestyle changes and the relevant mechanisms.

We will also continue to support research that examines the reciprocity of brain-body interactions in healthy aging and in the course of AD, especially interactions mediated by stress and other hormones. For example, short sleep—less than an average of 6 hours per night—has been associated with hormonal and metabolic changes that may lead to obesity, diabetes, hypertension, increased cardiovascular disease, or cognitive decline.

C-2 Develop better ways of distinguishing people with normal brain aging from those who will develop mild cognitive impairment, AD, and related conditions.

Successfully distinguishing people who are aging normally from those who will develop MCI—often a precursor to AD—and AD itself is critical to promoting healthy aging behaviors and the prevention, early detection and diagnosis, and treatment of disease. Identification of biomarkers of the transition from normal function to different levels of cognitive impairment is facilitating our efforts.

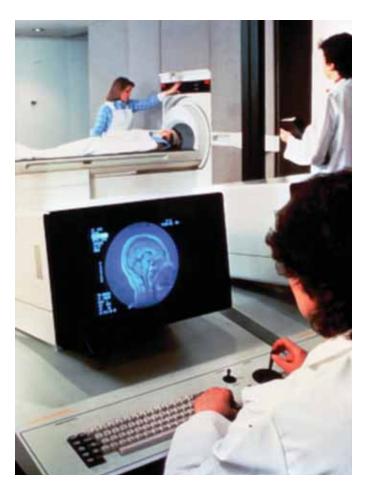
NIA will work to:

- Identify neuroimaging and other biological markers for early detection of cognitive decline, MCI, and AD and for understanding the progression from normal cognitive aging to MCI to early AD. Biomarkers may be helpful in earlier and more accurate diagnosis of disease and in tracking disease progression and treatment response in clinical trials, which can decrease the time and cost of trials.
- Improve neuropsychological assessment of cognitive function. Despite remarkable advances in neuroimaging, neuropsychological assessment of cognitive function continues to be the gold standard by which AD is diagnosed. We will continue to support development of better tools

- for assessing cognitive function in the clinic, in the primary care setting, and in the home environment. In one project, NIA helped establish the Uniform Data Set (UDS), comprising both clinical and neuropsychological tests, across all Alzheimer's Disease Research Centers (ADRCs) in the United States. The UDS will promote uniformity in collection of cognitive function data and will allow researchers to pool large sets of data across ADRCs. We will also participate in plans outlined by the recently funded NIH Neuroscience Blueprint Toolbox project to develop a measurement tool that includes a module for assessing cognitive, sensory, motor, and emotional function in adults. A standardized assessment tool of this type will help researchers track and compare behavioral change over time in longitudinal and epidemiological studies, in clinical trials, and eventually in primary care and other non-research settings.
- Improve methods of assessing changes in sensory and motor systems as markers of age-related change and AD. Age-related changes in sensory systems occur in both normal individuals and those with AD. We will continue to examine how the use of sensory testing to predict early neurodegeneration could assist in clinical diagnoses. We will also continue research to explore possible correlations between changes in sensory perception and AD. For example, we will investigate how changes in a person's ability to navigate visually through the environment or changes in a person's sense of smell may predict the development of AD.

C-3 Translate discoveries about the cellular and molecular mechanisms of cognitive, emotional, sensory, and motor function with age and the mechanisms of AD pathogenesis into diagnostic, treatment, and/or prevention strategies.

NIA-supported studies have combined both cognitive training and standard drug treatments such as donepezil to improve memory in patients with dementia. Other NIA-supported trials focus on slowing the progression of cognitive symptoms in dementia and on strategies to manage the behavioral symptoms. Still others focus on preventing the early stages of cognitive decline. NIA-supported translational studies apply the findings of basic science on brain mechanisms in healthy aging and in disease to the identification and preclinical testing of new prevention and treatment strategies as a precursor to testing in human clinical trials. A number of NIA-



supported trials focus on slowing the progression of cognitive symptoms in dementia and on strategies to manage the behavioral symptoms of dementia, while others focus on preventing the early stages of cognitive decline. Still others combine intervention strategies such as cognitive training and standard drug treatments (e.g., donepezil) to improve cognition in patients with dementia.

NIA will continue to:

- Stimulate translational research. We will continue to stimulate translational research aimed at discovery and preclinical development of new candidate drugs and biologics. By supporting the early steps of the drug discovery and development process, we can play a critical role in facilitating the very long, difficult, and enormously expensive process of translating the wealth of basic science discoveries into successful AD therapeutics. We will also support research to identify behavioral interventions aimed at maintaining brain and behavioral health and function during aging. We will apply what we are learning about the interplay among biological, behavioral, and social factors to develop more targeted and effective interventions.
- Support clinical trials for drug and behavioral interventions to prevent, treat, and delay the onset and progression of cognitive decline, MCI, AD, and other dementias. We will continue to support research to test promising new drug, behavioral, or combination interventions in clinical trials with the intention of moving them rapidly into clinical practice.

C-4 Conduct research to better understand and develop interventions to address the special caregiving needs of patients with AD and other dementias.

A number of recent studies have demonstrated that the chronic stresses of caring for a family member with dementia can cause lasting psychological and even physical consequences. These effects are multifold. For example, sleep-wake patterns are altered



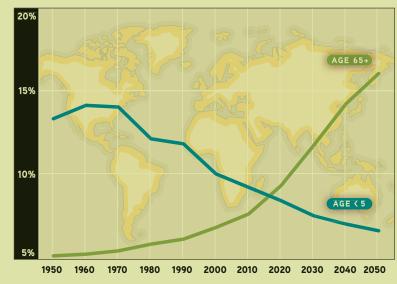
in AD patients, often leading to chronic sleep deprivation in the patients and their caregivers. Research has shown that caregivers of AD patients have an increased risk of depression, elevated stress hormones, increased vulnerability to influenza, and poor wound healing (in the older caregivers).

NIA will continue to:

■ Conduct research on the family and economic burdens of AD and other dementias. Formal and informal care for older persons with dementia is a major cost for families, private insurers, and the public sector. We will support research at several levels, including studies on the mechanisms through which the stress of caregiving affects health. We will work with others to develop new types of interventions for alleviating stress. Other studies will help us quantify and understand the economic burdens to inform health policy decisions.

Develop better strategies for the care of patients with MCI and AD and for alleviating caregiver burden. NIA-supported investigators have developed a multifaceted, personalized intervention that can significantly improve the quality of life for caregivers of people with dementia. We will continue to develop and test other interventions of this type. In addition, we will research the needs of long-term spousal caregivers following the death of their spouses and support development of post-bereavement interventions aimed at providing social support and working through the persistent traumatic and stressful thoughts of the prior years of caregiving.





Research Goal D

Improve our understanding of the consequences of an aging society and provide that information to inform intervention development and policy decisions.

The greater longevity and improved health seen at older ages in many parts of the world represent one of the crowning achievements of the last century, but also present a significant challenge. Societal aging may affect economic growth, patterns of work and retirement, the way families function, the ability of governments and communities to provide adequate resources for older people, and the prevalence of chronic disease and disability.

NIA will continue to support research on the social, economic, and demographic consequences of the rapidly aging population in the United States and other countries. In addition, we will continue to support research on how social and economic factors across the lifespan affect health and well-being during old age.

NIA's objectives in this area are to:

- D-1 Understand how population aging and changes in social, economic, and demographic characteristics of cohorts reaching old age affect health and well-being in the United States and other countries.
- D-2 Understand how social, economic, and health system factors produce disparities in health at older ages and develop interventions to reduce disparities.
- D-3 Understand how social and economic factors throughout the lifespan affect health and well-being at older ages.

D-1 Understand how population aging and changes in social, economic, and demographic characteristics of cohorts reaching old age affect health and well-being in the United States and other countries.

The social, economic, and demographic changes the Nation is experiencing at the population level may have profound effects on health and well-being at the individual level. For example, alterations in family structure may lead to changing trends in family caregiving practices, chronic diseases of aging may become more common, and the health care system may experience strain as greater numbers of Americans require services.

NIA will continue to:

Explore the effects of education and other social and demographic factors on health and well-being at older ages. Educational attainment is one of the strongest correlates of physical health and cognitive functioning at older ages. We will support research to unravel the reasons for this connection to help project health and long-term care needs and devise ways to intervene to reduce disparities.

- Assess the impact of changing family structures on health and caregiving. Changing family structures mean that people now approaching old age are more likely than their predecessors to be divorced, childless, or in stepfamilies. Researchers will need to examine how the presence of homeand community-based services (e.g., waiver programs, assisted living) influence the experience of family caregiving from an economic, social, and emotional perspective. Additional data are also needed to track the migration trends of older people as they move from community to community as well as from independent living to different levels of assisted living and nursing home care. We will support research on the ways in which the evolution of the American family structure will affect the well-being of the elderly by influencing living arrangements, caregiving, and economic support.
- Encourage comparative analyses to evaluate the impact of institutions on population and individual well-being and foster longitudinal studies on aging. Other countries have larger proportions of their populations now at older ages than the United States, and many of those with currently younger populations are aging at a much more rapid rate. A wide variety of institutional arrangements for income support, home health care, long-term care, and acute care have been developed in response to the challenges of population aging. We will support comparative research on the effects of these changes on behavior, and we will evaluate institutional reform efforts to gain insights useful both in the United States and elsewhere. We will also encourage analyses on the impact of global population aging on macroeconomic factors and their influence on institutions and well-being.

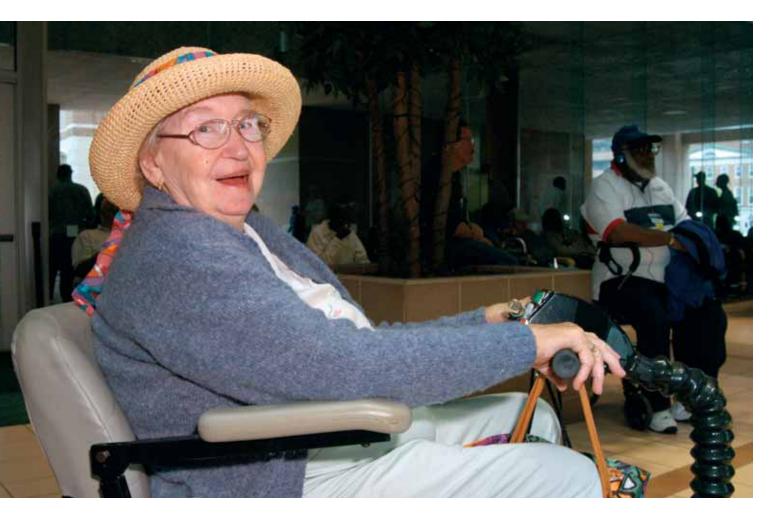
Understanding of Disability Trends Provides Insights for Effective Interventions

Disability rates among older Americans—the numbers of people unable to carry out, to specified levels, essential activities of daily living—have declined in recent decades, suggesting an improvement in health and function. *Activities of daily living* assessed in these studies generally include eating, dressing, bathing, toileting, and transferring from a lying down to a sitting or standing position. Researchers sometimes also examine "instrumental activities of daily living" like shopping or using the telephone.

The disability decline has been demonstrated in a number of studies, including the most recent U.S. National Long-Term Care Survey. This analysis revealed that the prevalence of chronic disability has dropped significantly from 1982 to the present. The continuing decline in disability among older people is one of the most encouraging and important trends in the aging of the American population. However, this trend may be threatened by rising rates of obesity and sedentary lifestyles in children and younger adults—both risk factors for late life disability.

Continued research on the causes of disability will inform the development and implementation of effective medical and behavioral interventions as well as public health programs to promote their use. For example, the Department of Health and Human Services uses health and disability trend information to create programs such as HealthierUS, a national effort to improve people's lives, prevent and reduce the costs of disease, and promote community health and wellness through physical activity, healthy diet, preventive screening, and cessation of high health risk behaviors such as cigarette smoking.

■ Develop a research plan to understand the dynamic changes that occur across the life course. Researchers will need to understand how experiences/exposures across the life course (infancy to older age) to a variety of environmental, intellectual, and social factors influence aging



and age-related well-being. We will examine factors contributing to maintenance or decrement of cognitive and physical functioning over the life course in an effort to forestall negative consequences and enhance health and well-being.

Examine the bases for individual and societal attitudes toward older people and develop effective strategies to improve them. Older people may be the target of inaccurate and negative stereotypes. We will support research to explore the causes of these negative attitudes and develop strategies to counter them with community and other interventions. For example, engaging older people in meaningful volunteer work may prove to be a "win-win" situation for society, replacing the image of dependence with one of active and productive citizens.

D-2 Understand how social, economic, and health system factors produce disparities in health at older ages and develop interventions to reduce disparities.

Health disparities continue to exist among racial, ethnic, and socioeconomic groups. Research is needed to understand the causes of these disparities and how they relate to social, economic, and health system factors and develop interventions to reduce the disparities.

NIA will continue to:

■ Encourage cross-national, comparative and his toric research as an approach to understanding the burden of disease and health disparities. Cross-national, comparative research using microlevel data has proven very useful in understanding how the structure of pension systems affects work and savings decisions.

THE SPEED OF POPULATION AGING

Number of years for population age 65+ to increase from 7% to 14%



Many countries have already reached the stage of population aging that is not expected in the United States until much later in the century, and many developing countries have populations that are aging faster than in the United States. Research on long-term trends in the burden of disease and risk factors can improve projections. Comparative research on the increasing burden of chronic diseases, and on ways in which families and health care systems cope with disease management and long-term care, could provide insights useful in the United States and globally.

Encourage interdisciplinary biodemographic, health systems, social, and economic perspectives to understand gender differences in health and disease at older ages. Recent demographic and economic trends have gender-specific implications for health and well-being at older ages. Nonmarried women, for example, are less likely than non-married men to have accumulated assets and pension wealth for use in older age, and older men are less likely to form and maintain supportive social networks. We will support research to explain how these and other factors may contribute to the differences in life expectancy and disability rates among men and women at older ages. This research will inform development of targeted policies to achieve dual goals of increasing longevity and delaying the onset and severity of disability.

D-3 Understand how social and economic factors throughout the lifespan affect health and well-being at older ages.

Individual differences in chances for a healthy and secure old age emerge in midlife. For example, NIA-supported research indicates that Americans in late middle age have much wider variation in wealth (i.e., total accumulated assets) than in current income (i.e., earnings). Furthermore, work and other decisions by people in their 50s and 60s are already affected by chronic conditions and disability. NIA-supported research will focus on both observational studies and interventions to improve function based on a life course perspective.

We will continue to:

■ Support research on social insurance and health insurance systems (e.g., Social Security and Medicare) to assist other agencies in promoting the health and well-being of the elderly while ensuring program efficiency. As record numbers of Americans reach retirement age, programs such as Social Security and Medicare will face unprecedented challenges. We will support research to assist these and related programs to work as effectively and efficiently as possible to safeguard the health and well-being of older Americans. Such research will include the measurement of the economic value of good health and the development of techniques to produce National Health Accounts. Our studies on the social, educational, public health, and biomedical variables that affect length of life and rates of disability, also will inform decisions related to social and health insurance systems. We will also support continued

- work to understand the biological, behavioral, economic, and social basis for decisions of individuals, employers, and families that affect income security in retirement and the financing of long-term care.
- Support research that models and measures the economic risks of old age with the potential for developing interventions to insure against these risks. Demographic and retirement income trends are expanding economic risks in old age. Higher life expectancy can increase the likelihood of outliving retirement savings, and the shift in pensions from defined benefit to defined contribution plans suggests that more Americans will reach retirement with Social Security as their only annuity. Although homes often represent the most significant part of retiree wealth, relatively few retirees make use of reverse mortgages to insure against retirement income shortfalls. Many Americans will require long-term care, but few purchase private insurance to support formal care expenses. Research that seeks to understand the behavioral aspects of demand for insurance against these old age risks and developing interventions that translate findings from behavioral research to improve well-being will be encouraged.



Research Goal E

Improve our ability to reduce health disparities and eliminate health inequities among older adults.

uring the 21st century, the United States will experience a dramatic increase in the proportion and diversity of racial and ethnic minorities in its older population. Life expectancy at older ages has increased significantly over the past 25 years but unacceptable disparities continue to exist in terms of disease burden and lifespan among racial and ethnic groups in the United States. Socioeconomic factors such as work, retirement, education, income, and wealth can have a serious impact on health and well-being. Economic circumstances can determine whether an individual can afford health care and proper nutrition from early life into old age. Individual and family financial resources and health insurance can determine whether an older adult enters a nursing home or stays at home to be cared for by family and friends.

Health disparities are associated with a broad, complex, and interrelated array of factors. Diagnosis, progression, response to treatment, caregiving, and overall quality of life may each be affected by race, ethnicity, gender, socioeconomic status (SES), age, education, occupation, and other as-yet-unknown lifetime and lifestyle differences. For example, a multi-ethnic epidemiological study supported by NIA indicated that prevalence rates for Alzheimer's disease may be higher for African Americans and Hispanics than for other ethnic groups. Another study found striking relationships between SES and both health and longevity. Gender differences in health and longevity also are observed across racial and ethnic groups.

We will continue to support essential research to increase our understanding of and reduce health disparities and inequities among older adults.

We will support research to establish the scientific basis for redressing differences and inequities affecting older adult populations. We will work to understand the extent to which genetic, behavioral, social, and other factors that show variation across racial and ethnic groups influence health and longevity. In addition, we will use new knowledge to develop behavioral and public health interventions for reducing disparities and increasing quality of life for all older adults.

Our objectives in this area are to:

- **E-1** Understand health differences and health inequities among older adults.
- **E-2** Develop strategies to promote active life expectancy and improve the health status of older adults in minority and other underserved populations.
- **E-3** Use research insights and advances to inform policy on the health, economic status, and quality of life of all older adults.

E-1 Understand health differences and health inequities among older adults.

There are many complex and interacting factors related to race, ethnicity, gender, environment, SES, geography, place of birth, recency of immigration, and culture that can affect the health and quality of life of older adults. Socioeconomic factors related to work, retirement, education, income, and wealth can have a serious impact on the health and well-being

of the elderly. Biological and genetic factors can also affect the course and severity of disease and disability. Furthermore, a person's culture can have a tremendous influence on health-related factors such as diet and food preferences and attitudes toward exercise. All of these factors and their interactions must be understood in order to design effective interventions to improve health equity among various ethnic/racial and low SES population groups.

To support this objective, NIA will continue research to:

- Understand normal aging processes across various ethnic/racial and low SES populations. We will characterize normal processes of aging in minority and low SES populations to increase our understanding of the course of disease and disability, and to identify the similarities and differences among racial and ethnic groups and among groups living in different geographic locations.
- Determine the effects of early life factors on adult health. Early life events can play an important role in the aging process. Differences in nutrition, education, disease incidence, environmental exposure and health care in fetal development and early life can affect disease and disability in later life. Research into the influence of early and midlife experience on the health of the aging will advance our ability to predict the health status of older adults in the future.
- Gather data that further classify patterns of health differences, inequities, and causes.
 - Compile data from multiple sources to assemble the necessary volume and types of information needed. Research to understand health disparities requires data that are accessible to researchers on a national level as well as appropriate ways

- to utilize multiple small data sets collected by many different researchers. NIA will support the use of these data to discover new scientific knowledge and to help in the evaluation and design of policies to deal with an aging society. This approach will allow data from several sources to be linked by a common identifier and analyzed in ways not previously possible.
- Use ongoing data collection programs to oversample minority populations. These data will provide important information on living arrangements, income, health care needs, and other topics.
- Continue to support surveys focused on specific groups and concentrated on issues of illness and well-being. NIA will continue to support and expand surveys of racial, ethnic, and language minority groups in order to provide the data needed by researchers and public policy makers.
- Determine the influences of and interactions among race, culture, ethnicity, economic status, education, and work experiences in health. Health and quality of life, particularly in later years, are affected by many interrelated factors. NIA will learn more about risk factors for disease and preventive factors contributing to good health by researching these influences individually and in concert. We will place a special emphasis on longitudinal data, which provide information about individuals across their lifespans, to untangle the multitude of factors that affect health and well-being.

E-2 Develop strategies to promote active life expectancy and improve the health status of older adults in minority and other underserved populations.

As life expectancy increases among all population groups, there are more adults living with one or more chronic conditions that may not affect the length of life but may dramatically affect quality of life. Research shows that these differences

Research Suggests a Positive Correlation between Social Interaction and Health

Several research studies have shown a strong correlation between social interaction and health and well-being among older adults and have suggested that social isolation may have significant adverse effects for older adults. For example, study results indicate that:

- Social relationships are consistently associated with biomarkers of health.
- Positive indicators of social well-being may be associated with lower levels of interleukin-6 in otherwise healthy people. Interleukin-6 is an inflammatory factor implicated in age-related disorders such as Alzheimer's disease, osteoporosis, rheumatoid arthritis, cardiovascular disease, and some forms of cancer.
- Some grandparents feel that caring for their grandchildren makes them healthier and more active. They experience a strong emotional bond and often lead a more active lifestyle, eat healthier meals, and may even reduce or stop smoking.
- Social isolation constitutes a major risk factor for morbidity and mortality, especially in older adults.
- Loneliness may have a physical as well as an emotional impact. For example, people who are lonely frequently have elevated systolic blood pressure.
- Loneliness is a unique risk factor for symptoms of depression, and loneliness and depression have a synergistic adverse effect on well-being in middle-aged and older adults.

More research is needed to understand the actual links to positive health and determine the importance of social interactions as they relate to disability, falls, memory, and overall health benefits for older adults.

in active life expectancy are more marked among the medically underserved. Genetic, lifestyle, and socioeconomic factors also play an important role in the time of onset or severity of disease and disability. NIA's efforts to understand the special needs of minority older adults will facilitate the design of effective interventions to improve health status and quality of life for our entire aging population.

NIA will continue research to:

- Track and analyze disease prevalence and course in diverse older adult populations.
 - Determine the causes of disparities in the prevalence of diseases and conditions such as heart disease, obesity, hypertension, frailty, diabetes, comorbidities, and certain types of cancer among minority and underserved populations. For example, African Americans suffer from hypertension and prostate cancer at higher rates than their white counterparts. Hispanics suffer more from diabetes but less from heart disease. NIA-supported researchers will explore socioeconomic factors such as education, language, and access to health care as well as how genetic, molecular, and cellular factors contribute to differences across populations.
 - Determine the reasons for variation in the prevalence of cognitive decline and AD across population groups. We will support research to better understand the differences in the prevalence of AD among African Americans, Asians, and Hispanics compared to non-Hispanic whites. For example, Japanese Americans living in Hawaii have lower prevalence of strokerelated dementia and higher rates of AD than Japanese nationals. We will continue to examine a range of possible causes of these disparities, including the impact of diseases such as hypertension, cardiovascular disease, and diabetes; health behaviors; and disease processes in minority populations. This research will draw on culturally appropriate, equivalent, and standardized measures to better understand these differences and to suggest culturally appropriate interventions.



Develop appropriate health strategies for disease, illness, and disability prevention and healthy aging among the underserved. Aging Americans need understandable, culturally appropriate interventions they can use to maintain and improve their well-being. For example, adults with low levels of education and limited fluency in English may need specially adapted assessments of cognitive function for the diagnosis of AD. Diet and exercise recommendations may need to be adjusted to take into account religious, ethnic, and cultural sensitivities. Adults are more likely to use their medication appropriately if the labels and instructions are printed in their native language.

To address these and other concerns, NIA will:

 Develop and promote culturally appropriate interventions to improve healthy behaviors along with strategies to increase the likelihood that these interventions will be initiated and maintained.

- Design and promote interventions appropriate for older adults in diverse populations to more effectively prevent, diagnose, or reduce the effects of disease.
- Design and promote culturally appropriate strategies for self management of chronic diseases.
- Investigate the factors affecting medication misuse and culturally appropriate strategies for enhancing proper use and compliance with medication regimens.
- Develop interventions to improve culturally appropriate health care delivery.
 - Design interventions to facilitate communication between health care professionals and Asian, Hispanic, and other elderly who have come to the United States with a range of educational and language skills. Interactions with health care professionals can be difficult if there are language and cultural barriers. If the elderly individual is hospitalized or placed in a nursing home, communication becomes a critical issue in ensuring appropriate health care. NIA will

- increase efforts to develop evidence-based practices that will facilitate communication of symptoms and care instructions between the patient and the health care provider.
- Develop interventions to reduce health disparities and inequities associated with poor providerpatient interactions. Recent studies have revealed that how older adults are diagnosed and treated is as much a function of who they are, who is treating them, and where care is provided as it is a function of the symptoms they present. NIA will investigate ways to ensure that each individual is treated with appropriate evidencebased interventions regardless of race, ethnicity, or cultural background.
- Develop strategies to increase inclusion of minorities and other underserved populations in research.
 - Investigate novel approaches for increasing representation and retention of minorities in research careers. We will work to identify the best strategies for training and attracting a diverse workforce of new, mid-career, and senior researchers for research on aging. We will continue programs to assemble a cadre of high-quality researchers through flexible training mechanisms that reflect the rapidly changing needs of science and provide crossdisciplinary training. We will work to tap the talents of all groups of society by encouraging degree-granting institutions to establish and improve programs for identifying, recruiting, and training women and men—including minorities and individuals with disabilities for careers in biomedical science. We will work to stimulate the training of investigators who can translate the findings of basic research into medical benefits for older people and expand the pool of clinical geriatric investigators.
 - Continue to support training for clinical staff in message development, recruitment strategies, and community and media outreach. Our ability to involve adults representative of the total

- population in research studies is essential to sound research and to obtaining the results needed for evidence-based intervention development. However, historically, members of minority populations have been underrepresented in clinical trials. Outreach efforts, such as involving faith-based and community organizations in emphasizing the importance of medical research and in recruiting study participants, have had varied success in minority populations. NIA will search for more effective ways to mitigate the difficulties associated with enrollment of minority individuals in research studies and clinical trials. For example, we will address cultural and language barriers and encourage effective communication of the potential benefits of studies and trials for improvement in health.
- Develop training programs to prepare culturally proficient service providers and researchers. We will facilitate training of researchers in the biomedical, behavioral, and social sciences as well as service providers working with older adults to help them better understand the medical implications of the growing diversity of our population. These training programs will help prepare the next generation of our health workforce by incorporating new materials sensitive to these issues.
- Conduct research to better understand effective strategies for communicating health messages that are culturally appropriate in various racial/ ethnic and low SES populations. Because of language, educational, and cultural differences, underserved groups do not always receive the information they need about healthy lifestyle behaviors. NIA-supported communication research with specific target audiences will assist the development of appropriate health messages and dissemination channels.

E-3 Use research insights and advances to inform policy on the health, economic status, and quality of life of all older adults.

A key resource for understanding health disparities and inequities that exist among older adults is data on trends and patterns that can explain the interaction between financial assets and health outcomes in different racial and ethnic groups and within economically disadvantaged groups. Data that increase our understanding of the role of educational status in improving health behaviors and health status will also inform the development of more effective policies.

Minority and underserved elders depend more heavily on Social Security, receive little support from private pensions, derive less income from accumulated assets, and rely to a larger extent on earnings from employment in old age. Challenges for policy makers include finding ways to encourage individual savings and home ownership and facilitate continued employment.

To support this objective, NIA will continue to:

- Study population changes and underlying causes of health and function of older adults across the lifespan. Many studies have identified significant risk factors for the development of chronic diseases that pre-date onset of symptoms by at least a decade. Population-based studies in which individuals are tracked from birth and across the lifespan help researchers understand the changes in health over time and the large variations in health across racial and ethnic populations. NIA-supported research will continue to develop, maintain, and analyze longitudinal data sets.
- Track and analyze patterns of aging and the burden of disease within and across diverse populations.

- Gather and analyze data on burdens and costs of illness, healthy life expectancy, longevity, and mortality trajectories. Determining the costs of specific illnesses has always been difficult due to the lack of adequate data on incidence and prevalence as well as inconsistencies in calculating direct and indirect medical costs. These difficulties are compounded in minority populations by differences in use of formal medical care and informal family caregiving. Projections of future active life expectancy, longevity, and mortality depend on assumptions about how groups of individuals will change over time, particularly as recent immigrants become culturally assimilated. This research will provide valuable information for projecting the specific needs for health care services within various population groups.
- Develop cross-national and sub-national databases on health outcomes, risk factors, and SES structural factors, such as societal inequality. Although many of the disparities in adult health and life expectancy across national, racial, occupational, and social class boundaries are well documented, causal mechanisms are less well understood. NIA-supported research to understand these differences will be critical to the development of behavioral and public health interventions.
- Provide information useful for policy discussion and decision making. We will continue to collect nationally representative longitudinal data on retirement, health insurance, savings, and family variables and share these data and trends with researchers, policy analysts, and program planners. Research findings of reduced disability among the elderly have become prominent in the public policy debate regarding Medicare and Social Security. NIA will investigate whether disability is being prevented or postponed, identify contributors to disability decline, determine the impact of changes in health care, and examine the economic implications of reduced rates of disability.

Partnerships Strengthen NIA Research Programs

The NIA research portfolio is broad based and includes research related to a variety of diseases and conditions relevant to the work of other NIH and outside organizations. This provides us with numerous opportunities to build synergy and leverage resources by partnering with other NIH Institutes and Centers (ICs), other government agencies, academic institutions, and professional and advocacy organizations.

We work closely with a number of other NIH ICs to co-fund research initiatives, support meetings and conferences, and develop educational materials. For example, we:

- Co-sponsor funding opportunity announcements across the full range of common programmatic themes.
- Collaborate with other NIH ICs on the NIH Roadmap for Medical Research initiatives such as the NIH Director's **New Innovator Award Program and** an interdisciplinary program in the behavioral and social sciences.
- Partner with other NIH ICs on NIH **Blueprint for Neuroscience Research** initiatives.
- Co-sponsor the Osteoarthritis Initiative with the National Institute of Arthritis and Musculoskeletal and Skin Diseases.
- Partner with the National Institute of Mental Health and the National Institute of Neurological Disorders and Stroke on the Cognitive and Emotional Health Project.

- Support the Study of Women's Health Across the Nation, a study of the menopausal transition, along with the NIH Office of Research on Women's Health.
- Partner with the National Library of Medicine to develop and maintain the NIHSeniorHealth Web site.

NIA also partners with other government agencies on several projects including:

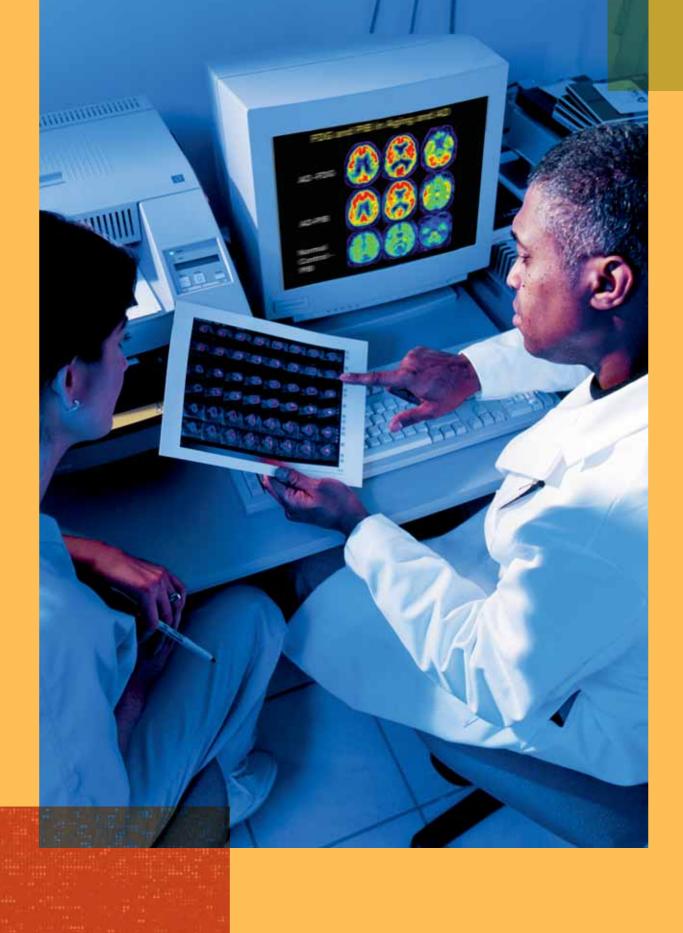
- Interagency agreements with the Center for Medicare and Medicaid Services and the Social Security Administration for collection and sharing of data through longitudinal studies such as the Health and Retirement Study.
- Collaborations with the National Center for Health Statistics, the Census Bureau, and others to compile and disseminate statistical information about aging.
- Partnerships to support meetings and conferences such as an international summit on global aging co-sponsored with the Department of State.

NIA's private-sector partners include:

 Nonprofit foundations and advocacy organizations. These include the Alliance for Aging Research, the Alzheimer's Association, the Alzheimer's Drug Discovery Foundation, the Alzheimer's Foundation of America, the American Academy of Orthopaedic Surgeons, the American College of Sports Medicine, the American Federation for Aging Research, the American Geriatrics Society, the American Society of

- Hematology, the Federation of American Societies for Experimental Biology, the **Foundation for the National Institutes** of Health, the Friends of NIA, the Gerontological Society of America, the **National Coalition for Osteoporosis** and Related Bone Diseases, and the Population Association of America and Association of Population Centers.
- Pharmaceutical, biotech, and related private-sector companies. These partnerships make tissues and other specimens, microarrays, rodent models, and other research resources available to investigators and support major initiatives such as the Alzheimer's Disease Neuroimaging Initiative, a joint effort involving NIA, the National Institute of Biomedical Imaging and Bioengineering, non-profit groups, and a number of pharmaceutical and biotech companies.

NIA also works closely with collaborators outside the United States to support studies to better understand the aging experience on a global level. For example, in the ongoing SardiNIA study, Italian and NIA intramural investigators have a unique opportunity to identify genetic and other risk factors for aging-associated conditions in a very stable population on the secluded island of Sardinia in the Mediterranean. NIA also co-funds more than two dozen cross-national, aging-related datasets and single-country studies of aging with partners like the World Health Organization.



Goal F

Support the infrastructure and resources needed to promote high-quality research and communicate its results.

he availability of the infrastructure and resources needed to support present and future research, program management, and information dissemination is critical to the NIA mission. NIA must provide resources to develop a skilled interdisciplinary research workforce, ensure that scientists have access to the technology and equipment they need to perform the research, and facilitate the dissemination of research results to scientists, health professionals, and the public. We have five objectives to support this goal.

F-1 Foster interdisciplinary exchange and encourage collaborative research across disciplines.

- Sponsor workshops and conferences that bring together scientists from various disciplines for discussion and planning.
- Provide funding opportunities that encourage interdisciplinary efforts with co-principal investigators and/or partnerships across two or more institutions or organizations.

F-2 Engage in partnerships to create synergy and leverage resources within and among institutions and organizations.

Work closely with other NIH Institutes and Centers, and other government agencies, to collaborate across the continuum of research from basic science through translational research to clinical studies and to disseminate information about proven interventions (research translation).

- Continue to participate in trans-NIH efforts such as the NIH Roadmap for Medical Research and the NIH Blueprint for Neuroscience Research.
- Partner with other government agencies, professional organizations, and advocacy groups to ensure that research results are translated into public health programs and medical practice and used to inform public policy.

F-3 Train and attract the diverse workforce of new, mid-career, and senior investigators necessary for research on aging.

- Develop and promote flexible mechanisms to meet the rapidly changing needs of science and prepare scientists, clinicians, and communicators to work effectively in interdisciplinary team environments across the continuum of research from basic to translational to applied.
- Develop partnerships with academia, professional organizations, and other entities to establish and improve programs for identifying, recruiting, and training scholars for careers in research on aging.
- Participate in efforts to recruit, train, and retain scientists across the full spectrum of research on aging, especially targeting under-represented groups.
- Encourage the training of investigators to translate the findings of basic research into benefits for older people.

F-4 Develop and distribute research resources.

- Support colonies of aged animal models, including genetically altered animals. These colonies are necessary for research on aging processes and specific age-related diseases.
- Make cell cultures and tissue, cell, and blood banks available for basic and epidemiological research.
- Create and make available DNA resources for genetic studies on aging and disease.
- Support access to imaging and other advanced technologies in shared facilities for examining aging biological systems.
- Support the development of population-based data sets, especially from longitudinal studies, suitable for analysis of biological, behavioral, and social factors affecting health, well-being, and functional status through the lifecourse.
- Support data archiving and data sharing, with adequate protections for confidentiality and privacy of research participants and their families.
- Support the development of internationally harmonized social and behavioral longitudinal data on aging to foster cross-national research.
- Support computer technologies to record and analyze interdisciplinary research findings on basic biological studies and long-term, population-based data.
- Support candidate drug evaluation programs, facilities, and related resources for animal and clinical studies.
- Develop innovative changes in the design, planning, and implementation of clinical trials and social and behavioral studies on the health and well-being of older people.



- Support a robust clinical trials infrastructure to facilitate the translation of basic research to human application in age-related diseases, and vice versa. This support will include technical assistance for patient recruitment and retention of older adults in clinical trials.
- Make results of research on patient recruitment strategies widely available to the research community.
- Support studies on the ethical aspects of research in older populations.

F-5 Disseminate information to the public, medical and scientific communities, and policy makers.

- Rapidly and effectively disseminate the latest advances in geriatric medicine, research on aging, and related health data through publications, professional education materials, public service announcements, and videos.
- Make available health information and reports of new research findings on the NIA Web site and through the NIA Information Center.
- Maintain and promote the NIA Alzheimer's Disease Education and Referral (ADEAR) Center and the NIHSeniorHealth Web sites.
- Develop materials for special audiences and diverse populations including non-English language materials and materials for people with limited literacy. Support national education campaigns to encourage healthy practices among older adults.
- Support innovative programs to promote positive attitudes toward older people's health needs on the part of health care and other service providers and the public at large.

NIA and NIH Web Sites Are Valuable **Sources of Health Information**

NIA Home Page - www.nia.nih.gov

NIH Home Page - www.nih.gov

NIA Publications - www.nia.nih.gov/HealthInformation

Alzheimer's Disease Education and Referral (ADEAR) Center - www.nia.nih.gov/Alzheimers

NIHSeniorHealth - www.nihseniorhealth.gov

NIA Spanish Home Page – www.nia.nih.gov/Espanol



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NIA Staff Contributors

- Richard Hodes, Judy Salerno, and Kathie Reed provided leadership for development of the document.
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Members of Our Research and Advocacy Communities

Individuals with the following organizations responded to our invitation to provide input to the NIA Strategic Directions during May and June of 2007: Alliance for Aging Research.

Alzheimer's Disease and Other Dementias Registry, New York State Department of Health. American Academy of Orthopaedic Surgeons. American Heart Association. American Psychological Association. American Society for Bone and Mineral Research. Association of Directors of Geriatric Academic Programs. Colorado State University. Directors of the NIA P30 Demography of Aging Centers. Harvard Medical School. Institute for Health Research - Kaiser Permanente. Institute for the Advancement of Social Work Research. Johns Hopkins University. National Association of Social Workers. National Sleep Foundation. Oregon Health and Science University. Orthopaedic Research Society. Population Association of America and the Association of Population Centers. Portland Veterans Affairs Medical Center. Saginaw Valley State University. School of Medicine -Virginia Commonwealth University. Sleep Research Society. Society of Clinical Geropsychology. Stanford University. The American Geriatrics Society. The American Society of Hematology. University of California. University of California - Davis. University of California - San Francisco. University of Illinois at Chicago. University of Maryland, Baltimore County. University of Massachusetts. University of North Carolina at Charlotte. University of Pennsylvania School of Medicine. University of Pittsburgh. University of Rochester Medical Center. University of Southern California. University of Washington. Veterans Administration Palo Alto Health Care System. West Virginia University. Western Suffolk/ Eastern Nassau Counties, Long Island, New York, Assisted Living Communities. Yale University.

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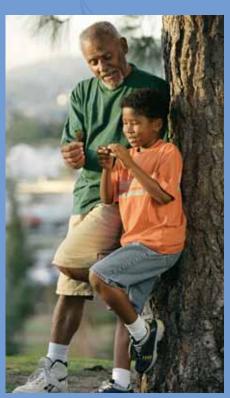
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