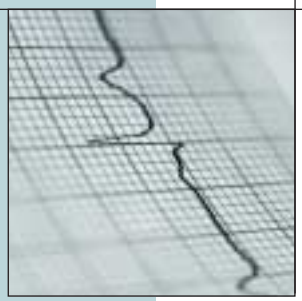
NATIONAL INSTITUTE ON AGING

ACTION PLAN FOR AGING RESEARCH:

STRATEGIC PLAN FOR FISCAL YEARS 2001-2005



National Institute on Aging
Strategic Plan for Fiscal Years 2001-2005

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Director's Message

Since its inception in 1974, the National Institute on Aging (NIA) has been supporting outstanding research to address the special problems and needs of older Americans and to improve scientific understanding of the aging process. In 1999, the NIA kicked off a year-long celebration of its 25th anniversary, providing a poignant and appropriate time for reflection on past achievements and future opportunities in the field of aging research. The NIA strategic plan is a document that encapsulates this crucial juncture in the history of the NIA and aging research, and presents a road map for the future.

The remarkable growth of the older population world-wide poses both opportunities and challenges. Notable progress in a number of areas of research—biomedical, social, and behavioral—have improved health and function, and contributed to reduced rates of disability, for older people. At the same time, unprecedented numbers of elders in the coming decades will face the risks of disease, frailty, and dependence. The need to understand the factors that promote health and independence and those that lead to disease and disability has never been more urgent. Fortunately, a strong aging research community is actively engaged in reducing the burden of disease and improving the quality of life of older people and their families.

In developing a new strategic plan for aging research, the National Institute on Aging has collaborated closely with the National Advisory Council on Aging and other public and private organizations to establish research priorities for the next five years. These priorities will address scientific topics that hold the greatest promise for advancing knowledge in areas such as the basic biology of aging, geriatrics, and social and behavioral functioning. Because the NIA is the lead agency for research on Alzheimer's disease, the NIA plan reflects its commitment to preventing and effectively treating Alzheimer's disease.

Richard Hodes, M.D.
Director, NIA

National Institute on Aging
Strategic Plan for Fiscal Years 2001-2005

Overview

The National Institute on Aging (NIA), one of the 25 institutes and centers of the National Institutes of Health (NIH), leads a broad scientific effort to understand the nature of aging and to extend the healthy, active years of life. This effort has rapidly expanded knowledge about the biological, behavioral, and social changes that occur with advancing age and has disproved stereotypes of inevitable decline as people grow older. Recent findings have revealed dramatic and unexpected reductions in rates of disability among older persons compared to projected levels. Millions of Americans are leading healthier lives based, in part, on discoveries from aging research.

Since the beginning of the 20th century, life expectancy at birth in the U.S. has increased from less than 50 years to more than 76 years. The challenge for the 21st century will be to make these added years as healthy and productive as possible and to maintain the current trend of decline in disability. There is no time to lose in discovering how to age well. From 1960 to 2000 there was an approximate doubling of numbers of people aged 65 and older. It is further projected that by the year 2030, the number of individuals age 65 and older will double again to reach 70.3 million, constituting 20% of the population. Dramatic growth is also projected in the numbers of Americans aged 85 and older, from 4.3 million (1.6%) in 2000, to 19.4 million (4.8%) in 2050—placing a significantly greater number of people at risk for disease and disability. It is urgent to develop more effective treatments for age-related diseases and to prevent or delay the onset of disease and disability among older persons. Evidence shows that health research is making progress toward both these goals.

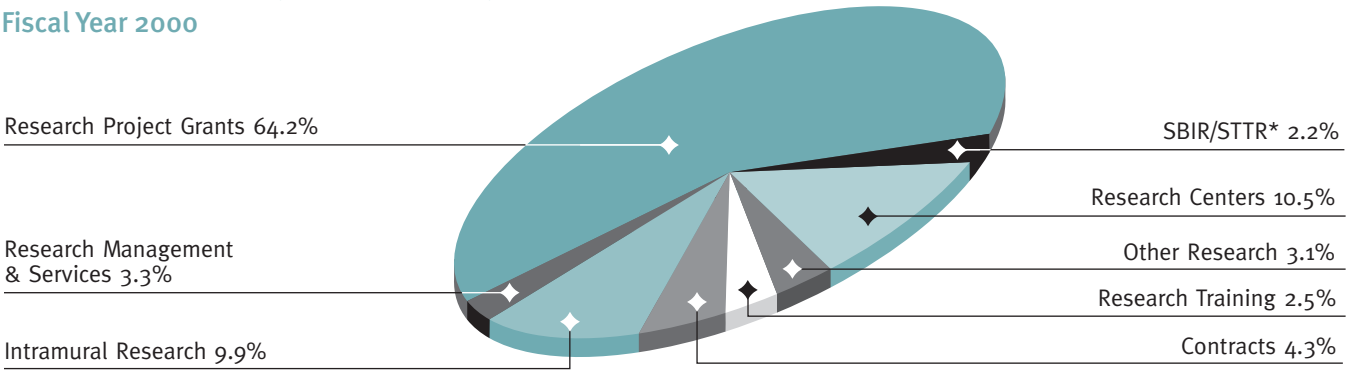
NIA Mission. In 1974, Congress granted authority to form the National Institute on Aging to provide leadership in aging research, training, health information dissemination, and other programs relevant to aging and older people. Subsequent amendments to this legislation designated the NIA as the primary federal agency on Alzheimer's disease (AD) research. The NIA's mission is to improve the health and well-being of older Americans through research, and specifically to:

- Support and conduct high quality research on:
  - aging processes
  - age-related diseases
  - special problems and needs of the aged
- Train and develop highly skilled research scientists from all population groups
- Develop and maintain state-of-the-art resources to accelerate research progress
- Disseminate information and communicate with the public and interested groups on health and research advances and on new directions for research.

NIA Funding and Collaborations. The NIA has fostered progress in aging research for over 25 years. In fiscal year 2000, the NIA funded basic and clinical scientists through an estimated 1,400 research grants and 55 research contracts to universities and other research centers, supporting investigators throughout the U.S. and in selected international locations. Investigators also apply for training grants and individual fellowships. The NIA now provides support to approximately 526 scientists-in-training and to senior investigators who are learning new disciplines in aging research. The Institute also supports a broad range of research by NIA scientists in its own (intramural) laboratories. Distribution of funds for these activities is shown in the figure on page 3.

The NIA collaborates with every major NIH component and leads research efforts that span several federal agencies. The NIA is the lead federal agency for research on Alzheimer's disease and aging demography. In this capacity, the NIA chairs the NIH Inter-Institute Alzheimer's Disease Working Group to promote research development, coordination of funding, information dissemination, and other matters of common interest. The NIA also chairs the Interagency Ad Hoc Committee on Research on Aging and the Interagency Forum on Aging Related Statistics. In addition to areas in which NIA has lead responsibility, many of the diseases and concerns

National Institute on Aging
Distribution of Funds by Budget Category
Fiscal Year 2000



* Small Business Innovation Research (SBIR)/Small Business Technology Transfer Research (STTR)
NIA Budget 9/00

TOTAL NIA: $685,695,000

that affect the health of older people are the primary responsibility of other NIH institutes and centers. In these cases, the NIA collaborates with these organizations to advance knowledge of aging and leverage resources. Other collaborations involve research on cardiovascular disease, cancer, neurologic diseases, osteoporosis, osteoarthritis, diabetes, AIDS, behavior and health, and alternative medicine.

NIA Research Planning. The NIA maintains a year-round scientific planning process that draws upon interactions with scientists throughout the world, members of Congress, the Institute's National Advisory Council on Aging (NACA) and other advisory committees, constituency groups, and the public. These interactions stimulate internal consideration of potential new research strategies and provide a broad perspective for refining plans. Emphasis is given to novel proposals and collaborative projects that promise to stimulate activities with other research organizations.

The NIA's strategic planning process focuses on a 5-year planning horizon. The most recent strategic plan, developed by the Task Force on Aging Research in 1995, produced a comprehensive research agenda through fiscal year 2000. The NIA's current strategic planning effort covers a 5-year time frame from fiscal years 2001 to 2005 and addresses goals for research, research training, research resources, and dissemination of health information. Members of the scientific community and the general public have been active in the plan's development.

The plan addresses four major goals:

- Goal A **Improve Health and Quality of Life of Older People**
- Goal B **Understand Healthy Aging Processes**
- Goal C **Reduce Health Disparities among Older Persons and Populations**
- Goal D **Enhance Resources to Support High Quality Research**

Research goals A, B, and C represent broad areas that NIA will pursue in the years to come. They are not meant to be mutually exclusive, and there are many areas of overlap and interdependence. For example, knowledge gained from basic research can lead to clinical interventions that improve health and quality of life and in turn reduce health disparities among population groups. Advances in one area of science can provide clues and new directions for another area of investigation. To complement these three goals, Goal D will help ensure that aging research benefits from a strong infrastructure to support future research, program management, and information dissemination.

A Research Goal

Improve Health and Quality of Life of Older People

As life expectancy increases, there is an ever greater need to keep these additional years free of disease and disability. Research has shown that lifestyle and other environmental influences can profoundly impact outcomes of aging, and that remaining relatively healthy and emotionally vital into very advanced ages is a realistic expectation.

NIA research is helping to identify lifestyle factors and health behaviors that directly influence physical and mental fitness and risk of disease. Scientists are defining optimal recommendations regarding diet, dietary supplements, exercise, safety, and other factors to ensure health and function and reduce the risks of disease and disability. People of all ages can use this knowledge to increase the likelihood of enjoying a healthy old age.

Strategies are being developed to prevent or reduce the severity of health problems in older people and improve health and long-term care. One approach is defining the gradual or programmed changes in structure and function that characterize normal aging. Understanding how these changes impact on health may lead to innovative means of disease prevention and therapy. Another approach is discovering the pathologic changes that precede or occur with disease. These advances are essential for early diagnosis and present opportunities for stopping or reversing the course of the disease.

Efforts also are underway to enhance elders' physical, mental, and interpersonal abilities and to expand opportunities for achieving personal goals and contributing to society. This research will identify behaviors and social interactions that influence health and quality of life. Results of these studies can enhance symptom management, conserve function, and improve caregiving.

Improving health and quality of life for older adults therefore depends upon progress in achieving three research objectives:

- Prevent or reduce age-related diseases, disorders, and disability
- Maintain physical health and function
- Enhance older adults' societal roles and interpersonal support, and reduce social isolation.

Subgoal 1:

Prevent or Reduce Age-Related Diseases, Disorders, and Disability

Remarkable progress is being made through basic, clinical, and epidemiologic research toward developing innovative, safe, and effective approaches to prevention and therapy for the population over age 65. These studies seek to improve vaccine and drug development, lessen the disabling effects of disease, delay onset or progression of disease, and enhance pain management.

Aging research targets diseases and conditions that contribute significantly to mortality or disability in old age. A major focus of NIA research is Alzheimer's disease, a devastating neurodegenerative disease that robs people of memory and other intellectual abilities, leading to loss of social and occupational function and ultimately to complete dependence on others. Additional important causes of disease and disability include cardiovascular disease and cancer, the two leading causes of death in older people; bone, muscle, and joint disorders such as osteoporosis and osteoarthritis that contribute to pain and loss of mobility; vision, hearing, and other sensory disorders that can isolate older people; and numerous other age-related conditions, such as diabetes and incontinence, that deprive individuals of their independence.

To reduce the burden of illness and disability in older people, researchers in aging are capitalizing on new findings to:

a. Accelerate discovery of causes and risk factors, and improve early detection and diagnosis of disabling illnesses.

Genes associated with aging processes, longevity, and age-related diseases are providing insight into disease pathologies and individuals' vulnerability to disease. Defining the underlying changes in biologic functions controlled by the genes can lead to possible targets for treatment, and may help in early detection and diagnosis of disease. These findings are derived in part from studies of populations or families known to be at high risk for a disease. Population studies also uncover other potential risk factors, such as environmental exposures across the life span, health behaviors, and the influence of coexisting conditions on the progression of a disease. In addition, remarkable progress is being made through advances in imaging technology, a non-invasive means of observing the body's biological activity. For example, these techniques can provide images of nerve cells as they communicate, can accurately measure cerebral blood flow, and can gauge the production of particular gene products. Plans are being developed to improve the resolution of this technology to assist in early detection and diagnosis.

b. Discover new treatment and prevention strategies.

New information on the underlying causes of and risk factors for diseases and disabilities are helping researchers develop interventions to delay onset, slow progression, and reduce the severity of disease and disability. Insights have emerged from studies on alterations in genes or gene products, effects of hormones or other factors external to the cell, and changes in how the body coordinates and integrates its complex activities. These studies have produced promising targets to prevent death or inappropriate proliferation of cells and to reduce inflammation and damage to tissues. Researchers are actively translating new knowledge on genetics, biochemistry, and physiology to develop new preventive strategies and medications. Studies are being considered for tissue repair and cell replacement using stem cells, immature cells that can differentiate into specialized cells to replace those lost due to normal cell turnover or injury. Clinical trials are needed to identify more effective strategies for rehabilitation to improve function and quality of life and to overcome barriers to optimum function. Behavioral and social science findings are also

being applied to develop strategies that promote health and prevent disease.

c. Improve health behaviors and medication use.

Exercise, proper diet, and other healthy behaviors can help prevent and reduce symptoms of disease. These benefits often rely on an individual's willingness to make and sustain changes in lifestyle. Researchers are exploring strategies that can help motivate elders to adopt changes that promote health and adherence to medical recommendations.

Managing medications can be complex for older people, who may take several drugs for multiple health problems. Complications may occur because of interactions between two drugs or between a drug and dietary supplements, or because of physiological and functional changes associated with aging or age-related diseases. Planned research will provide new knowledge about medications to maximize their effectiveness and will develop new technical aids to assist physicians in monitoring drug use. New technologies and information will enable patients to better manage drugs and avoid adverse reactions.

d. Launch clinical studies to improve health and reduce burden of disease.

New clinical studies are being developed to improve treatment of Alzheimer's disease, cardiovascular disease, cancer, osteoporosis, and diabetes, and to test the effects of hormone replacement, dietary supplementation, and exercise and fitness. As pathways and processes of disease are defined, basic research findings can be translated expeditiously to clinical applications. These studies will test new drugs and compounds, strategies for improving physical and mental fitness, or approaches for preventing falls and other injuries. Several novel approaches are being applied to make these studies as efficient and

cost-effective as possible. Every effort is being made to ensure participation of diverse populations. In addition to efforts to prevent disability among healthy older persons, studies will also focus on reducing disability and/or preventing or slowing additional decline among persons with disability as they continue to age.

e. Strengthen infrastructure and resources required for clinical trials and other clinical studies.

Until recently, elders have been markedly underrepresented in clinical trials—even in some of the disorders most prevalent in older men and women. An invigorated program of clinical studies in older people is designed to produce:

- Innovative changes in the design, planning, and implementation of clinical trials. For example, a special effort will be made through the Alzheimer's Disease Prevention Initiative, which will be discussed later in this section.
- New drug testing facilities and resources, such as an intramural Interventional Trials Unit to translate laboratory research findings to human findings in several age-related diseases and in immunology and endocrinology.
- An expanded collaboration with the Veterans Administration Cooperative Studies Program to study osteoporosis and hormone replacement therapy in older men, nutritional interventions in vulnerable geriatric populations, multifactorial interventions to prevent fall-related fractures, and other topics.

- New efforts with the National Cancer Institute to improve cancer therapy in older people, including the effects of aging and co-existing conditions on responses to and side effects of surgery, chemotherapy, and radiation therapy.

Research on Selected Geriatric Diseases, Disorders, and Conditions

To achieve these objectives, the NIA has developed specific initiatives in several geriatric diseases, disorders, and conditions, including:

- Alzheimer's disease and other degenerative diseases of the nervous system, and age-related changes in memory
- Major geriatric concerns, including weakness and falls, delirium, urinary incontinence, sleep disturbances, depression, and comorbidities
- Cardiovascular disease
- Cancer
- Diabetes
- Bone, muscle, skin, joint and movement disorders
- Vision, hearing, and other sensory disorders
- Benign prostatic hyperplasia
- Infectious diseases

Alzheimer's Disease. The NIA is the lead federal agency for studying Alzheimer's disease (AD). As many as four million Americans suffer from AD, the most common form of dementia. This brain disorder gradually progresses from mild memory loss to disturbing changes in behavior and personality, decline in the ability to think or recognize people, and profound memory loss. Gradually and inexorably, AD consumes and destroys normal brain function. Patients eventually are unable to care for themselves and sometimes are agitated to the point of causing harm to themselves or others. Both patients and the millions of family members and other loved ones who care for them are devastated by AD.

These profound losses are related to abnormal changes in the brain that begin many years before memory loss or other clinical symptoms become apparent. Major breakthroughs in genetic, molecular, and epidemiologic research are rapidly expanding our understanding of these pathologic changes. Researchers are precisely characterizing the regions of the brain, such as the hippocampus, that are involved in memory and other cognitive abilities. In AD, brain cells in these regions die in unusual numbers. Efforts are being made to inhibit loss of neurons, for example, by increasing protective growth factors in the brain. Communication among brain cells in AD patients begins to break down as synapses, the communication points between neurons, are lost. Scientists are exploring ways to prevent this loss. Investigators are also tracking the formation and potential interaction between the two major lesions—amyloid plaques and neurofibrillary tangles—that proliferate in the brains of Alzheimer's patients, with the aim of finding ways to stop their formation, reduce their numbers, and minimize deleterious downstream effects.

Remarkable progress has been made toward a more complete understanding of the agents that damage cells and the subtle changes in cellular function that can trigger cell death in the brain. AD can also interact with other diseases, such as cardiovascular disease and stroke, to make symptoms worse. These findings suggest targets for new diagnostic, preventive, and therapeutic strategies for AD. In addition, these advances will certainly lead to insights about other diseases in which nerve cells die, including Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis and non-AD dementias.

Alzheimer's Disease Prevention Initiative

The Alzheimer's Disease Prevention Initiative strives to prevent AD and to slow disease progression once it is diagnosed. This initiative will intensify collaborative efforts to conquer AD between NIA and other NIH institutes, several government agencies, organizations such as the Alzheimer's Association, pharmaceutical companies, and private foundations. Goals are to:

- **Accelerate discovery of new risk and protective factors, and identify promising targets for preventing disease through basic research.**

Potential targets for slowing or stopping the course of AD have multiplied as knowledge of the causes and early predictors of the disease increase. Several genes have been discovered that can cause AD and other dementias in certain families that develop these diseases in early to middle age. Progress in understanding the function of these genes has led to a surge in knowledge about the development of AD pathology, including proliferation of senile plaques and neurofibrillary tangles, and has stimulated efforts to block or even reverse the progression of these pathologies.

Investigators are now better able to detect persons at high risk for developing AD. Powerful genetic tools have helped reveal genes, such as APOE ε4, that influence susceptibility and disease progression in late-onset AD. These discoveries not only improve ability to identify persons who have a greater chance of developing AD, before the disease causes damage to the brain, but also lead to new avenues of drug development as the basic mechanisms underlying disease progression are revealed.

Developments in brain imaging and in cognitive testing are enabling researchers to identify people at ever earlier stages of the disease and to characterize brain and behavioral changes that precede clinically diagnosed dementia. For example, a brain imaging study of the size of the hippocampus in older individuals with mild cognitive impairment (a memory deficit beyond that expected for age and education) found that the smaller the hippocampus at the beginning of the study the greater the risk of later conversion to AD. These diagnostic advances will open new opportunities for early interventions to prevent brain changes before clinical deterioration occurs. Research is also producing a number of candidates for diagnostic markers; appropriate markers would enable physicians to accurately distinguish AD from other dementing illnesses as well as from age-related loss of function.

Molecular and epidemiologic research has made progress in identifying possible new targets for drug therapy. These targets include inflammation and toxic oxidative agents known as free radicals. Another possible problem that could be corrected is loss of protective factors, such as estrogen or natural growth factors.

- **Speed drug discovery and movement of promising new treatments and prevention strategies into clinical trials.**

To invigorate drug development, novel proposals are being solicited to target crucial pathways involved in the development of AD. Research has led to the threshold of discovery of effective agents targeting AD pathology. For example, researchers have succeeded in developing agents that retard deposition of brain plaques in animal models. Another promising research area is development of estrogen-like compounds that retain estrogen's beneficial effects on the brain while minimizing its negative effects on other organs. Yet another is development of molecular compounds that prevent brain cells from dying or stimulate the generation of new brain cells. Ultimately, as a long-term goal, methods may be developed to introduce cells into the brain that could either protect brain cells from AD damage or even replace dysfunctional cells.

- **Launch clinical trials to prevent AD.**

Unlike trials that focused on reducing symptoms and slowing the progress of AD, many future trials will emphasize prevention of the disease. Advances in basic research and drug development are likely to include more effective anti-inflammatory compounds and anti-

oxidants, agents to prevent cell death, and substances designed to stop the deposition of plaques and tangles in the brain. Such progress will enable more effective intervention at earlier stages in pathogenesis. The first NIH prevention trial, comparing the effects of vitamin E and Aricept was recently initiated at more than 70 sites in persons diagnosed with mild cognitive impairment but not clinical AD. Aricept helps prevent the degradation of acetylcholine, a brain cell communication chemical important for attention and memory. Vitamin E is thought to have antioxidant properties that counteract damage from molecules called oxygen free radicals. The goal is to stop the development of AD symptoms in these individuals, who are at high risk of developing AD. Other trials involve estrogen; non-steroidal anti-inflammatory drugs; cerebrovascular interventions; and a folate, vitamin B6, and vitamin B12 combination. Efforts are also being made to develop sensitive tests and techniques that can quickly and accurately track a drug's effectiveness in slowing or arresting brain changes that precede or accompany the progression of AD. Over the next several years, not only will trials be conducted among persons with mild cognitive impairment, but also in persons with completely normal cognition in order to prevent AD prior to emergence of any symptoms.

- **Expand strategies for improving patient care and alleviating caregiver burdens.**

There is a critical need to develop more effective methods to treat and manage behavioral symptoms in persons who have AD and to significantly reduce caregiver burdens. Focused initiatives will develop and test new ways of managing the daily activities and stresses of caring for people with AD, with focus on behavioral symptoms most distressing to AD patients and their families: wandering, aggression, agitation, sleep problems, and incontinence. Clinical studies of behavior management strategies, both pharmaceutical and behavioral, also will be launched. Successful treatment of AD will help prevent hospitalizations, decrease unscheduled visits to care providers, delay nursing home admission, avoid preventable illnesses unrelated to AD, and prevent caregiver burnout.

Major Geriatric Concerns. A number of conditions compromise independence and quality of life in older persons. These conditions result in increased suffering, service utilization, and health related costs. Research will be expanded to address the following geriatric concerns:

- **Weakness and falls** result in approximately 1.5 million fractures each year, including debilitating fractures of the hip and spine. Muscle weakness, bone loss, dizziness, and impaired mobility contribute to falls and other injuries. New strategies are needed to reduce the risk of falls through health promotion and patient education, safety measures, environmental modifications, and improved therapies.

- **Delirium**, also known as acute confusional state, is a serious and preventable cause of suffering and service use among elderly people. A recent study showed that hospitals may be able to reduce the number and duration of episodes of delirium in at-risk older patients by addressing specific risk factors. Research is aimed at preventing delirium by understanding and reducing these risk factors—which include cognitive impairment, sleep deprivation, medication error, immobility, visual and hearing impairment, and dehydration.

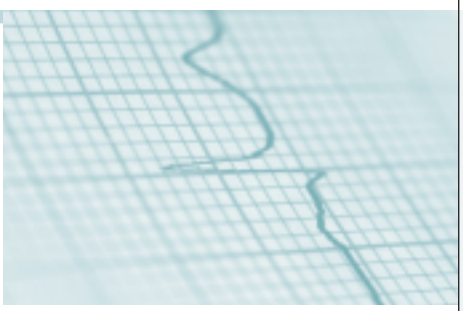
- **Urinary incontinence (UI)**, a significant medical problem with physical and psychosocial ramifications, affects up to one-third of women over age 65. Studies have shown that medications, surgery, and behavioral approaches can be effective in treating some women with UI. The need remains for additional research on the underlying causes of UI, on development of new, safe treatment methods, and on educating elders and health professionals about the condition.

- Studies suggest that **sleep disturbances** afflict a majority of the older population in the U.S.,

contributing to personal discomfort and illness and caregiver burden. Contrary to a commonly held belief, however, chronic insomnia, which occurs in about a third of our elderly population, is not a normal consequence of aging. To reduce the burden of sleep disturbances, scientists are studying the mechanisms underlying sleep-wakefulness cycles, normal and abnormal bio-rhythmicity of the aging nervous system, and the effects of concurrent disease states on sleep. Planned research should contribute to developing new and more effective therapeutic methods that will correct the underlying pathology of sleep disorders to improve quality and duration of sleep in older persons.

- **Serious depression** is an important public health problem in older people that may occur along with other common medical conditions. Often overlooked or misdiagnosed, clinical depression can affect cognition and exacerbate physical, mental, and emotional problems. In collaboration with the National Institute of Mental Health, research will continue to refine and develop diagnostic screening tests for depression in older adults, and to develop more effective medications with fewer side effects.

- **Comorbidities** and their influence on function, health and treatment must be better understood. The risk of multiple diagnoses increases with advancing age, leading to concerns regarding interactions among diseases, interactions between a drug given for one disease and a co-existing disease or condition, and drug-drug interactions as diseases are treated. Efforts are also underway to improve strategies for including in clinical trials persons with comorbidities so that the effects are better understood for the types of drugs most likely to be prescribed for the elderly.



Cardiovascular Disease. Diseases of the heart and blood vessels are the leading cause of hospitalization and death in older Americans. Congestive heart failure is the most common diagnosis in hospitalized patients aged 65 and older. The NIA is pursuing a broad program of basic and clinical cardiovascular research, often in collaboration with the National Heart, Lung, and Blood Institute. Recent findings have demonstrated the effectiveness of both pharmacologic and lifestyle approaches in reducing hypertension and preventing heart disease and stroke. Characterization of age-associated changes in both the structure and function of the heart and blood vessels is vital to the development of newer, more effective treatment and prevention interventions. Research priorities include genetic and environmental risk factors for hypertension, heart disease, and stroke. Studies are ongoing to determine the causes of age-associated increases in vascular stiffness, a potential risk factor for cardiovascular disease. Other research will focus on age-related changes in the structure and function of the heart's conduction system that can increase the risk of cardiac arrhythmias, especially atrial fibrillation; if uncorrected, this condition can lead to strokes. Additional priorities include determining the reasons for gender and racial differences in the aging cardiovascular system, delineating the relationship of cardiac enlargement to aging and disease development, and reducing the progression of early atherosclerotic disease.

Cancer. The second leading cause of death among the elderly is cancer, with individuals age 65 and over accounting for 70 percent of cancer mortality in the U.S.

In collaboration with the National Cancer Institute (NCI), the NIA is expanding basic and clinical research on breast, prostate, and colon cancers, common in older people, and launching a new initiative to expand participation of older cancer patients in clinical trials. This research focuses on age-related changes that contribute to increased cancer incidence and mortality in older persons, aggressive tumor behavior in the aged patient, and the impact of previous or concurrent conditions and disabilities on the cancer experience of older patients. Specific research topics include: dose adjustment for anti-tumor agents and radiation therapy, diagnostic cancer imaging, how coexisting diseases affect cancer treatment and survival outcome, and survival advantages or disadvantages of minority or ethnic populations.

Diabetes. Type 2 diabetes, which results from insulin resistance and abnormal insulin action, is most prevalent in the older population. Diabetes complications, such as heart disease and loss of sight, increase dramatically when blood sugar is poorly controlled and often develop before diabetes is diagnosed. Working with the National Institute of Diabetes and Digestive and Kidney Diseases, the NIA is exploring strategies to prevent type 2 diabetes and to expand knowledge on usual age-related increases in insulin resistance and glucose tolerance. Studies are also focusing on how changes caused by type 2 diabetes affect responses to treatment and prevention strategies in older persons. Other studies will develop critical resources to study genetic susceptibility and gene/environment interaction in type 2 diabetes.

Bone, Muscle, Skin, Joint and Movement Disorders. Osteoporosis (loss of mass and quality of bones), osteoarthritis (inflammation and deterioration of joints), and sarcopenia (age-related loss of skeletal muscle mass and strength) contribute to frailty and injury in millions of older people. Several initiatives, some in collaboration with the National Institute of Arthritis and Musculoskeletal and Skin Diseases, are unraveling the underlying mechanisms of aging in bone, muscle, skin, and joints with the goal of conserving or enhancing their function and preventing pathologies. For example, factors are being explored to define the influences that can predispose older people to fractures and develop effective prevention and intervention strategies for age-related musculoskeletal decline. Also contributing to loss of mobility and independence are changes in the central nervous system that control movement. Cells may die or become dysfunctional with age, as in Parkinson's disease. Older people therefore may have difficulty with gross motor behavior, such as moving around in the environment, or with fine motor skills, such as writing. Research is being conducted to understand the underlying age-related changes that occur in the motor control areas of the brain with the aim of developing therapeutic interventions. One such approach, deep brain stimulation, is being pursued as a collaborative effort with the National Institute of Neurological Disorders and Stroke.

Vision, Hearing, and Other Sensory Disorders. Age-associated changes in sensory function, including vision, hearing, taste, smell, proprioception, and vestibular function, can lead to significant loss in function, as well as decrease the quality of life for many older persons. In collaboration with the National Institute of Deafness and Other Communication Disorders, and the National Eye Institute, progress is being made in discovering risk factors for age-related hearing loss and vision decline. Increased emphasis is being given to research on multiple sensory deficits in older people, which increases their risk for mortality and loss of independence. Ongoing research is redesigning products and developing new technologies for older people to make reading easier and more understandable, enhance hearing and other sensory abilities, and otherwise contribute to functional independence. Age-related declines in taste and smell may have an impact on both the enjoyment and nutritional choices of the elderly. Studies on flavor enhancement are aimed at maintaining healthful eating habits, especially in sick and otherwise debilitated elderly. Understanding the mechanisms involved in decreased sensory function is also expected to lead to interventions to maintain optimal function into the later years.

Benign Prostatic Hyperplasia. It is common for the prostate gland, part of the male reproductive system, to enlarge with age. More than half of men in their 60s and as many as 90 percent in their 70s and 80s have some symptoms of this condition, known as benign prostatic hyperplasia or BPH. Symptoms stem from obstruction of the urethra (the canal through which urine passes out of the body) by the adjacent prostate gland. Severe BPH can lead to urinary tract infections, bladder or kidney damage, bladder stones, and incontinence. Although some researchers believe that factors related to aging may spur development of BPH, the cause is not well understood. The NIA stimulates research on the causes of the high incidence of prostate growth in older men and on issues related to treatment and potential regimens to minimize prostate growth.

Infectious Diseases. The mechanisms that underlie the decline of immune function often accompany advancing age, leaving older people more vulnerable to conditions such as influenza and pneumonia. Success in understanding changes with age in immune competence and the underlying mechanisms of these changes have broad implications for vaccine development and reduction in infectious illness, which often leads to hospitalization and death in older people. An emerging research focus involves prevention of HIV/AIDS in older people, a growing health problem. NIA research on these issues is coordinated with the National Institute of Allergy and Infectious Diseases and the NIH Office of AIDS Research.

Subgoal 2:

Maintain Health and Function

Older Americans are relatively healthy and independent, with a large proportion free of disabilities. Many older persons lead fulfilling lives and continue to make important contributions both within their families and to society in general. Achieving and maintaining health and function in advanced years can be aided by a commitment to a life style that promotes fitness, proper nutrition, and avoidance of smoking and other behaviors that adversely affect health. Even if healthy habits have been neglected, research has shown that it is almost never too late to begin these habits. Better health habits not only help people survive longer but postpone the onset of disability and compress functional loss into fewer years at the end of life.

Recent research has shown that disability levels for people age 65 and older have been falling at an accelerating pace since 1982, and that the benefits of this trend extend both to men and women and to minority groups. This decline contributes to improved functional ability for individuals and could have important economic and social implications. The need to maintain or accelerate this decline is urgent. By the year 2030, the number of Americans over age 65 will more than double, and by 2050, the number of Americans over age 85 will increase four-fold or more, placing a significantly greater number of people at risk for disability. Extending the current level of disability decline over the next 50 years could prevent increasing the number of disabled Americans in the face of the demographic challenge posed by the baby boom and overall population aging.

Initiatives are being developed to:

a. Understand declines in disability rates for older persons.

In order to sustain continued decreases in disability, it will be critical to identify the social,

educational, public health, and biomedical variables that affect length of life and rates of disability. Recent studies have identified trends that are likely to extend the disability decline, such as the increasing education levels of older people, improvements in health-related behaviors, improvements in the availability and effectiveness of assistive devices, and improvements in the treatments of conditions that lead to disability. Based on the explanatory factors identified, additional research will consider interventions that could enhance the disability decline. Efforts also will be made to improve projections of disease and disability rates and to clarify the implications of improving health for medical care costs. Unless we can better understand the disability decline and find ways to reduce disability, we may be faced with a significant increase in the numbers of disabled elders.

b. Improve strategies for promoting healthy behaviors.

Diet. It is generally accepted that nutrition has a direct bearing on health in elders. Healthy diets have shown the potential to lower blood pressure and blood cholesterol, and studies are underway to determine the efficacy of various diets to prevent cancer, diabetes, and other conditions in older people. General recommendations for healthy eating in young or middle age may not be optimal for older people. More research is needed to uncover the basic mechanisms that underlie changes with advancing age in nutritional requirements such as for vitamins, minerals, fats, and proteins. Special dietary concerns related to difficulties that occur during aging in digesting food and absorbing nutrients at the cellular level, and adverse interactions between drugs and nutrients, need to be further explored. It is also unclear what weight is ideal in old age; this question is under study. Additional research attention must be given to the role of diet in preventing the progression of existing diseases and conditions in order to improve health outcomes and personal function.

Smoking and Alcohol Abuse. The harmful health effects of smoking and alcohol abuse are well documented. Studies have shown that people at any age can benefit from quitting both of these habits. Research is needed to improve strategies for encouraging behavioral changes to quit smoking and use alcohol only in moderation in later years.

Safety. New studies have shown that evaluating risk factors and making alterations in home and work environments can reduce falls and their consequences. Human factors research is discovering new ways to improve safety in the home and community and remove physical barriers and obstacles. Progress is also being made to identify factors that put older drivers at risk of automobile crashes. Research will continue to identify safety risks for older persons, improve screening strategies, and develop information to reduce risk.

Exercise. Exercise can help delay the onset of disabilities and life-threatening diseases, reduce the risk of falls and fractures, improve mood and relieve depression, and may increase life expectancy. Exercise can improve mental acuity. These benefits are accessible even to the very old. Many physically frail people 90 years and older can more than double their strength through simple exercises in a fairly short time. Nevertheless, many Americans—especially older Americans—are not engaging in regular, sufficient physical activity. NIA supported research is expanding our understanding of the benefits of physical fitness as well as the factors that motivate and deter people from making exercise a part of their daily routine. Studies will also focus on relating exercise to positive health outcomes and understanding exercise physiology and other basic science aspects to maximize exercise's positive effect on older people.

c. Evaluate hormone replacement therapy and dietary supplements.

Counteracting the 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 knowledge of their safety is known. Although levels of these hormones may decline, on average, as people age, maintaining the former levels may not be needed as a person grows older. Even if effective, supplementation may entail risks. For example, estrogen supplementation can be successful in combating osteoporosis and may have beneficial effects on brain function and memory. But estrogen replacement therapy may increase the risk of stroke and breast cancer. More research is needed to determine how the biologic action of these hormones changes in older people and to assess whether replacement of these hormones will improve health.

Alternative approaches are also needed to realize the benefits of estrogen, testosterone, and other hormonal therapies while minimizing risks and undesirable side effects. Two principal strategies are being pursued. One involves synthesizing related compounds that produce the beneficial responses of hormones in the body without detrimental side effects. Another approach is to regulate hormone production in specific body tissues where increased or decreased amounts of these hormones is favorable to health. When successful, for example, these innovative approaches will enable men and women to benefit from the properties of estrogen without its unwanted side effects.

Research is also underway on the ability of anti-oxidants such as vitamins C and E to prevent cancer, delay aging, or keep cognition intact. Antioxidants are found in common foods and act as scavengers for oxygen radicals, molecules generated when cells produce energy, that can cause long-term harm and degradation to the body. NIA research will address the special dietary and nutrient needs of elderly persons, especially nutrients capable of delaying or mitigating the degenerative diseases that often accompany aging.

d. Improve elder interaction with the health system.

Research is benefiting health outcomes by helping to improve the quality of interactions among doctors, other health care providers, patients, and families. Research to enhance care and communication will lead to improved patient self-management, higher levels of patient satisfaction, and better health outcomes. It is also important for older individuals to recognize the implications of disease-related signs and symptoms and to consult a physician or other health care provider when they first occur. This consultation is neglected in many cases. Older people also frequently fail to report symptoms to their physicians. According to one study, fewer than 40% of persons who experienced symptoms associated with heart and circulation or musculoskeletal systems sought a physician's care. Similarly, women often avoid seeking care for urinary incontinence. Future research will help ensure that elders will appropriately seek medical advice and assistance.

e. Reduce caregiver and family stress and improve individual coping with chronic disease.

Families and individuals who care for people with chronic disease may routinely face emotional stress as well as physical and financial burdens. Investigators are also evaluating strategies to

improve social support, skills training, and assistive services for caregivers and others who cope with chronic disease. Research will provide information on needs and patterns of family caregiving and on how people make decisions on providing care. Research will also improve guidance on support and skills, and will include a focus on families with diverse backgrounds.

Subgoal 3:
Enhance Older Adults' Societal Roles and Interpersonal Support, and Reduce Social Isolation

Social support and continued involvement in useful activities have been shown to foster positive effects on health and longevity. In contrast, studies have associated lack of social connectedness with significant increased risk for poor health and death. Being part of an active network also increases the opportunity for productive activities, whether paid or volunteer. For most older men and women, a substantial amount of productive work and contributions continue throughout life. Identification of valued roles and continued social integration have been associated with positive health outcomes and self-assessed well being. Similarly, other aspects of health behaviors and lifestyles have been associated with important health outcomes.

Close links have been established between lifestyles and health outcomes. We hope to learn how to ensure that people will initiate beneficial behavior changes, and also sustain these choices over the long term. This effort is especially important for older individuals, who are at increased risk for multiple pathologies, disability, and functional limitations, which may keep them from fully engaging in the world around them.

Improvements in acute and long-term health care for older people are 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 strategies for prevention, treatment, and rehabilitation.

Objectives include:

a. Identify ways for older people to retain valued roles and maintain independence.

Despite negative stereotypes, millions of older people contribute to keeping our society functioning and loathe the thought of being a burden. Most older men and women are now working in paid jobs, doing essential volunteer work, maintaining a household, and/or supporting children and grandchildren. For example, according to one source, if family caregivers had to be replaced, an estimated three million paid workers would have to be recruited. Research is helping to optimize the unique resources that elderly citizens represent. Investigators are seeking and applying technological, social, and behavioral findings to extend older people's ability to remain independent, active, and productive in later life.

b. Enhance family functioning.

Intergenerational family support accounts for the way the family assembles and allocates its resources—money, skills, and time—to care for all its members. Research is needed to monitor these relationships over time; to understand both their effects on the health and well-being of older people; and to gain insight into the caregiving, emotional support, and economic transfers provided by older people. More research is needed to address the important issues of increased demands faced by the family's caregivers in light of the changing patterns of work and family demographics, including such characteristics as gender, marital status, income, wealth, education, race, and ethnicity.

c. Reduce elder neglect and abuse.

Although isolated studies have documented the devastating long-term consequences of elder

mistreatment, research on elder abuse and neglect is seen as inadequate, as noted by a recent study by the Institute of Medicine, National Academy of Sciences. Substantial research is needed on the prevalence of elder abuse, on reliable measurement tools for assessing elder abuse by health care professionals, and on interventions to reduce the incidence of elder abuse.

d. Improve health care and long-term care.

There is a pressing need to define organizational mechanisms that will assure quality, affordable health care for the elderly. Attaining this goal will require examining component parts of health care delivery systems and their impact on medical, social, functional, and cost outcomes. An important research focus will involve coordination of care to promote attention to patient and family preferences, smooth transitions between care settings, and maximize independence.

For long-term care, most often provided in a home setting, research can be helpful in reducing the burdens of caregivers, with an emphasis on the unique challenges faced by dementia caregivers. Studies are planned to fill gaps in our understanding of caregiving patterns and the effectiveness of different strategies for helping families manage care needs of physically frail elders. For both informal and formal long-term care settings, specific guidance is being developed on caregiving skills, environmental modifications, and technological supports.

e. Improve end-of-life care.

There is a critical lack of empirically generated knowledge on how to maximize quality of life at the end of life. Medical culture is oriented primarily to patient care and not to addressing the multifaceted needs of dying individuals and their families. Future research should focus on the impact of health care organizations and provider interactions on the quality of life for dying individuals. Special attention

should 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. Also needed to improve older people's experience at the end of life is research on: the transitions among end-of-life care settings such as the home, hospital, nursing home, and hospice; better measures of the quality of life at the end of life for both the patient and his or her family; and the social and economic context of caring for a dying elder.

f. Enable elders and families to prepare for and cope with age-associated changes in health, income, and function.

Older adults and family members are faced with many complex decisions about retirement, finances, health and life insurance, and medical treatment. In addition are issues associated with the ability of health care delivery systems to support patient and family needs and adherence to patients' advanced directives. To inform decisions about issues of health, finances, and family in late life, NIA studies are developing up-to-date information about patterns of work and retirement, sources of retirement income, intergenerational income transfers, and status of health and disability. Research will also be used to improve information and other resources for persons planning for later life transitions.

Research Goal B

Understand Healthy Aging Processes

Subgoal 1:

Unlock the Secrets of Aging, Health, and Longevity

Research on the biology of aging has led to a revolution in aging research. New findings about the factors that affect aging have begun to provide valuable insights about longevity and the genesis of disease.

No single theory can account for all the changes that take place as people age. Aging today is viewed as many processes, interactive and independent, that determine life span and health. These dynamics result in wide variations in aging both among individuals and among different biological processes and systems within the body. Understanding these variations and their causes promises to translate into interventions that extend the proportion of our lives spent in good health.

Chronic diseases and disabilities were once thought to be inseparable from aging. This view is changing rapidly as the means are developed to prevent, treat, or control diseases. If chronic disease is not intrinsic to aging, then what is "normal" aging? Normal or usual changes with aging, just like diseases, are influenced by genetics, environment, and lifestyle. The link between genes and life span is no longer questioned. For example, selective breeding in fruit flies has resulted in flies that live nearly twice as long as average. In addition, recent studies of human centenarians have found that extreme longevity runs in families, suggesting a strong genetic influence on aging. Complementing the genetic influences on aging are the strong effects of environmental factors, such as toxins, radiation, and oxygen radicals—highly reactive molecules produced as cells turn food and oxygen into energy. Progress is being made in understanding and counteracting these environmental effects. Lifestyle choices, including diets, physical activity, and other health habits, as well as behavioral and social factors, also have a potent effect on aging processes.

To understand the normal or usual changes with age, NIA's goals are to:

a. Identify factors that pace the aging process and slow the clock.

Caloric restriction is the only intervention known to reliably extend the healthy life span of rodents and nearly all other non-primate laboratory animals studied. Fed 30 to 40 percent fewer calories than in usual feeding schedules, but given all the necessary nutrients, the animals studied have lived far beyond their normal life spans. Animals on restricted diets also have reduced rates of several diseases, especially cancers. Laboratories are now studying caloric restriction in non-human primates. So far, researchers have identified changes in physiologic function in calorically restricted rhesus monkeys that are associated with delays in aging-related decline in animals. Further studies of caloric restriction will help identify the fundamental reasons for the increase in longevity and reduction in disease and thus uncover the mechanisms responsible for disease in old age.

To understand the biologic mechanisms involved in this phenomenon, researchers recently examined 6,500 mouse genes and identified 58 genes that actively produced (or expressed) more than twice as much gene product at older ages. These genes were involved in stress responses and growth of neurons. The major effect of caloric restriction seems to be to heighten animals' stress response to damage to proteins and other large molecules.

Most cells have a finite life span—after a certain number of divisions specific to the cell type, they enter a state of cell senescence, no longer dividing, their ability to synthesize DNA blocked. This built-in limit on cell division may help explain the aging process. Several genes have been identified that regulate senescence, some of which trigger cell proliferation and others that counter cell division. Research into what causes cells to mature, to lose the capacity to reproduce, and eventually to die promises to provide valuable insights about the genesis of disease.

Telomeres have been regarded as the cell's "molecular clock." These protective segments of DNA on the ends of chromosomes shorten each time most types of cells divide until, at a critical length, cell division ceases. Major advances recently have been made in understanding the role of telomeres. The enzyme telomerase compensates for telomere shortening by adding DNA segments to the ends of chromosomes, enabling cells such as sperm to divide indefinitely. How telomerase activity in cells contributes to cancerous growth is not known, but many scientists view telomerase inhibition as a potential new approach to cancer therapy. In a recent experiment that inserted the gene for telomerase in normal, telomerase-negative cells, shortened telomeres grew longer, and the cells replicated far beyond the limits observed for normal cells while retaining the function of young, normal cells. This advance not only suggests that telomeres are the central timing mechanism for cellular aging, but also demonstrates that such a mechanism can be reset. Controlled activation of telomerase may provide an avenue for healthy cell division by resetting or extending the timing of the molecular clock.

Oxygen radicals are known to attack proteins, cell membranes, and DNA. The body has a multilayer defense system of antioxidants which react with and disarm these molecules. Vitamins C, E, and beta-carotene can function as antioxidants, along with enzymes such as superoxide dismutase and catalase. They can prevent most, but not all, oxidative damage, and one theory contends that this accumulation of damage results in malfunctioning of genes and other aging-related changes in tissues and organs. Researchers are actively pursuing research on the effects of oxygen radicals, the body's antioxidant defenses, and the use of antioxidants as dietary supplements. DNA also is assaulted by ultraviolet (UV) light and other toxic agents. The ability of an organism to detect and repair certain types of DNA damage is believed to be directly related to the life span of the organism. Scientists have found DNA repair defects in people with a genetic susceptibility to cancer, and hope to discover the role of DNA repair in the increased risk of cancer in older people. Researchers are also studying other processes that contribute to the rapid and efficient response to stress crucial for a healthy, long life.

b. Define the biologic and environmental factors that maximize cognitive, sensory, and physical functions.

Research has contributed insights into the interactions between the brain and the peripheral nervous system, endocrine system, and the immune system. Findings from these studies will have an important impact on preventive and therapeutic approaches to maintain health in cognition, sleep, and sensory processes.

Hormones are the body's chemical messengers, stimulating specific functions within the body. Researchers have long known that some hormones decline with age. Growth hormone levels decline, as do levels of the sex hormones, testosterone and estrogen. The most familiar example of this phenomenon is the decline of ovarian hormones that accompanies menopause. When some declining hormones are replaced, various signs of aging diminish. Estrogen replacement therapy after menopause not only alleviates unpleasant symptoms unique to menopause, but also lessens the accelerated loss of bone characteristic of osteoporosis, and

may help prevent cardiovascular disease. There also is evidence that estrogen replacement may have a positive effect on cognition. The changes specific to the menopause, other hormonal changes with age, as well as hormone supplementation are being investigated to help define the role of hormones in health and disease and the potential benefits for hormone supplementation.

The ability of the immune system to protect people from infection also undergoes a gradual decline with age. Exciting progress is being made in understanding the complex defenses that are mounted against invading bacteria and other foreign cells and the interactions of hormones with the immune system. Prevention of declines in immune function would make a significant contribution to improving the health span and quality of life of older people. New knowledge in this area has broad implications for improving vaccine efficacy and other prophylactic techniques against infection, as well as reducing infectious diseases, the cause of much hospitalization and death in older people.

Personality factors also have been shown to have a significant impact on health and survival. New findings are helping to understand the links between personality and health. For example, health can be affected by how conscientious a person is in eating well or taking medication. People with personalities prone to high anxiety and other negative emotions can suffer from stress, which induces the manufacture of neurotransmitters—messengers of the nervous system—and hormones designed to aid the body in responding to dangerous or stressful situations. These hormones can damage cells, tissues, and systems in the body. There is evidence from animal studies that elevated stress hormones can lead to cell death in the hippocampus, which is rich in receptors for the stress hormone cortisol.

Age-associated changes in sensory function, including vision, hearing, taste, smell, proprioception, and vestibular function, can lead to significant health and functional problems and significant decrease in quality of life for older persons. Relatively simple lifestyle changes can lower the risk for some sensory declines. Not smoking and living in a smoke-free environment can lower the risk of hearing loss and wearing plastic lenses or hats with brims can reduce cataract risk by lowering eye exposure to UV-B from sunlight. Understanding the mechanisms involved in decreased sensory function is expected to lead to interventions to maintain optimal function into the later years.

c. Identify genes associated with aging, longevity, age-related diseases, and behavior.

Research has begun to reveal the biologic factors associated with extended longevity in humans and animal models. Within the last 10 years, numerous genes have been implicated in normal aging processes, in age-related pathologies and diseases, and in determination of longevity in several species, including humans. Some of these genes are associated with dramatic extension of life span in tiny worms called nematodes, in fruit flies, and in mice. Using advanced technology, the NIA plans to accelerate its efforts to discover additional age- and longevity-related genes and to characterize their biological function.

A new initiative will extend studies of longevity-associated genes, changes in gene expression patterns, and the genetic epidemiology of human longevity. The ultimate goal of this effort is to develop interventions to reduce or delay age-related degenerative processes in humans.

Revolutionary advances in the fields of quantitative and molecular genetics hold great promise in the search for the genetic determinants of complex behaviors. Twin studies in humans can help identify the relative contributions of environment and heritability to dementia, cognitive abilities, physical functioning, well-being, and social aging. New techniques can track the developmental course of genetic contributions to behavior, identify genetic heterogeneity, and explore genetic links between the normal and abnormal.

d. Identify social, psychological, and lifestyle factors that promote health, well-being, and longevity.

Just as psychological and lifestyle factors have been associated with preventing disease and disability (as described in Goal A), similar factors are being identified that are associated with "successful aging." By this we mean not simply avoiding disease but rather achieving full potential and vitality in later years. Research into behaviors and health promotion strategies to achieve well-being in later years will include reducing stress and other risk factors for disease and disability, keeping the mind and body well exercised, and maintaining a vigorous involvement in activities of life.

e. Disassociate changes of normal or usual aging from those of diseases and disorders.

A special effort is needed to disentangle the normal or usual changes with age from those of disease and disability. Individual health providers and family members have to make difficult distinctions, for example, between age-associated changes in memory and early AD. Clearer information about how a disease presents in older individuals would help avoid missing a diagnosis such as depression. Changes associated with normal aging also affect the rate and experience of disease and disability and may exacerbate symptoms. Many patients experience multiple problems that complicate diagnosis, treatment, and rehabilitative services. New knowledge will be developed to distinguish among and better understand usual aging, disease, and disability, stimulated by advances in imaging technology and genetics, clinical studies, and improvements in information dissemination.

Subgoal 2:

Maintain and Enhance Brain Function, Cognition, and Other Behaviors

In the past, significant loss in the ability to remember, learn, think, and reason—skills known collectively as cognition—were considered a normal part of aging. Now we know that most people remain both relatively alert and mentally able as they age and that severe cognitive loss is the result of disease. Without disease, older people can maintain mental acuity by taking part in activities that stimulate the mind and the body. Remaining actively and productively engaged in one's community and social group, and leading a healthy lifestyle are important in maintaining optimum brain function. Severe mental decline is not inevitable; the aged brain maintains the capacity to make new connections, absorb new information, and acquire new skills.

Some losses in memory and other aspects of cognition do occur with advancing age. Being able to distinguish between normal changes and the abnormal changes of disease is crucial for diagnosing disease and for designing strategies to maintain cognitive function. This knowledge is being developed by studying changes in areas of the brain involved in learning and memory, such as the hippocampus.

New methods of imaging the activity of specific regions of the brain allow scientists to see the brain at work during cognitive tasks and thus help identify age-related neural changes and ways in which the older brain attempts to compensate in order to maintain optimal cognitive function.

Knowing how the brain ages provides important information on which to base strategies for maintaining and enhancing cognition through biological and behavioral interventions. For example, it was recently shown that some new neurons form in adulthood in certain regions of the brain, contrary to prevailing beliefs. This advance presents the possibility that methods could be found to compensate for neuron loss and cognitive decline from disease or traumatic injury. Behavioral strategies are also being developed to retain cognitive function.

To maintain cognition and avoid disease and disability, research is needed to:

a. Characterize changes that occur with normal brain aging and with neurodegenerative disorders.

Scientists are making significant progress in understanding what constitutes normal brain aging. Contrary to earlier beliefs, decline in neuron number is not significantly involved in normal brain aging. In fact, recent evidence indicates that the older brain is capable of generating new nerve cells, particularly in a region of the brain important for acquiring and processing information, the hippocampus. These findings have turned researchers' attention to the investigation of more subtle neural changes with age: selective neuronal loss or dysfunction with implications for memory and other functions, remodeling of synapses (where nerve cells communicate), reduction in or dysfunction of neuronal connections, minor brain atrophy, and changes in responses of non-neuronal cells (such as glial cells) involved in neuron survival and brain plasticity. Modest decline also has been detected in the chemicals that conduct nerve signals, such as acetylcholine, and in communication among brain regions.

In neurodegenerative disorders, neuronal cell death and dysfunction are widespread. Gene mutations result in altered proteins that cause or contribute to disease. Abnormally-folded, insoluble proteins may accumulate in the brains of patients. These changes are often correlated with the proteins' losing function or becoming toxic, leading to death of neurons. Neuronal death may also occur because of inappropriate activation of a signaling pathway for "cell suicide," known as apoptosis. Synapses decrease in vulnerable areas of the brain. Glial cells may become activated, contributing to inflammation. Further characterization of these pathologic changes will enhance our basic knowledge of altered neural function in the elderly and aid the development of appropriate treatments.

b. Characterize normal cognitive and brain function of the oldest-old.

Very little is known about the changes in brain function that normally take place in the fastest growing segment of the U.S. population—the oldest-old—those individuals aged 85 years and older. In the absence of disease, many of these individuals continue to lead healthy and productive lives even into extreme old age. It is important to distinguish normal aging-related changes from disease in this group in order to find ways to maintain function as long as possible.

Another growing segment of the population is made up of centenarians, those individuals aged 100 or more. Scientists are studying this group to understand what factors or behaviors contribute to their long lives, especially among those who continue to function well.

c. Understand the interaction of gene, molecular, cellular, and environmental factors for optimal cognitive function.

Promoting the full potential of the central and peripheral nervous systems depends on developing the brain optimally in early life, continuing cognitive activity to maintain function, and stimulating the brain to compensate for cell death and injury. More needs to be learned about neurotrophic factors, protein signals that promote growth and survival, and their impact on stimulating the brain to adapt to declines in function. Research is underway to find the genetic, cellular, and molecular basis of functional decrements in nervous system aging. Strategies must be developed to minimize environmental factors, such as oxidative stress and toxins that degrade function. New leads for optimal nutrition for nervous system development early in life and maintenance in later life should be identified to improve cognitive processes and delay age-related mild cognitive impairment.

d. Enhance learning, attention, memory, language skills, reasoning, judgment, decision-making, and other aspects of cognition.

Interventions designed to improve cognitive or related perceptual abilities and skills can reduce the need for formal care and hospitalization, and maintain independence for older people. Everyday tasks that use inductive reasoning can be taught by demonstrating strategies to identify rules or patterns or by practicing problem solving. These tasks include ensuring that older persons can complete a medication schedule chart or load a pill reminder, understand schedules, follow menus, engage in work or leisure activities that involve following a pattern or rule, and perform repetitive exercise routines. Regular challenges of the brain can help retain cognitive abilities and mental acuity. Research with such practical applications for improving everyday functioning will be encouraged.

Research Goal C

Reduce Health Disparities Among Older Persons and Populations

Health disparities are associated with a broad, complex, and interrelated array of factors. Risk factors, diagnosis, progression, response to treatment, caregiving, and overall quality of life may each be affected by aspects such as race, ethnicity, gender, socioeconomic status, age, education, occupation, and as yet unknown lifetime and lifestyle differences. For example, a recent multi-ethnic epidemiologic study indicated that prevalence rates for AD may be higher for African-Americans and Hispanics than for other ethnic groups. Another study found a striking relationship between socioeconomic status (SES), health, and longevity. Gender differences in health and longevity are observed across racial and ethnic groups. Understanding these differences and interactions is critical for developing behavioral and public health interventions to reduce burdens of illness and increase quality of life.

Subgoal 1:

Increase Active Life Expectancy and Improve Health Status for Older Minority Individuals

In the next half century, the proportion of racial minorities and Hispanics among the elderly population is expected to increase rapidly and become more diverse. Life expectancy at older ages has increased significantly in the last quarter century for all major racial groups, although there are disparities. More marked differences among these racial and ethnic groups exist in "active life expectancy," the average number of years lived without a limiting disease or disability. Improved diagnosis and treatment of major medical conditions have led to growth in the number of persons living with one or more chronic conditions which impact not necessarily on the length of life, but on the quality of life. Genetic, lifestyle, and socioeconomic factors also play an important role in the severity or time of onset of disease and disability. It is important to understand the special needs of minority elderly persons in order to design appropriate interventions to improve health status and quality of life for all older persons.

a. Analyze disease prevalence and course in minority populations and sub-populations.

The prevalence of many diseases, including heart disease, hypertension, diabetes, Alzheimer's disease, and certain types of cancer, vary significantly among minority populations. For example, blacks suffer from hypertension and prostate cancer at higher rates than their white counterparts, while Hispanics have more diabetes and less heart disease. Scientists still do not understand all of the factors involved in these health disparities. Differences in the prevalence of Alzheimer's disease in blacks and Hispanics compared to non-Hispanic whites may be related to socioeconomic factors, including education, language, and access to health care, biological factors such as the higher incidence of cardiovascular disease in African-Americans, and genetic factors such as different prevalence of risk factor genes in these populations.

Different prevalences or frequency of declines in cognitive function have been observed among populations. This may, in part, be due to stress-related diseases, such as hypertension, cardiovascular disease, and diabetes. Despite the substantial evidence that these diseases affect cognitive functioning, there are scant relevant data examining minority and ethnic populations. Future research will focus on studies of cognitive functioning, health behaviors, and disease processes in minority populations using culturally equivalent and standardized measures, to better understand these differences and to suggest culturally appropriate interventions.

Research also will focus on determining the factors contributing to the differences in the prevalence of Alzheimer's disease among different racial and ethnic populations. For example, Japanese-Americans living in Hawaii have lower prevalence of stroke-related dementia and higher rates of Alzheimer's disease than do Japanese nationals. Data are needed on the specific incidence and prevalence rates in different ethnic sub-populations as well as the distribution of subtypes of dementia, genetic and environmental risk factors, and differences in caregiving.

b. Increase inclusion of minorities/sub-populations in research.

Historically, members of minority populations have been underrepresented in clinical trials. There are many difficulties associated with enrollment of minority individuals in research studies and clinical trials. Cultural and language barriers must be overcome, as well as finding ways to inform individuals of the studies and trials that are available and their potential benefits for improvements in health. Outreach efforts, such as involving church and community organizations in emphasizing the importance of medical research and in recruiting

study participants, are very important for minority elderly. Research on improving strategies to include minorities in research as well as direct efforts to recruit minorities to clinical studies are underway.

c. Develop preventive and interventional strategies for healthy aging appropriate for diverse populations.

In order to prevent or lessen the effects of disease, interventions must be designed that are culturally appropriate. For example, minority elderly individuals are more likely to use their medication appropriately if the labels and instructions are printed in their native language. Interactions with health care professionals can be difficult if there are language and cultural barriers. In order to diagnose Alzheimer's disease in minority elderly, assessments of cognitive impairment must be designed for individuals with low levels of education or lack of fluency in English.

Future research will focus on strategies for self-management of chronic diseases such as arthritis, heart disease, lung disease, and diabetes. Research also will investigate the factors affecting medication misuse and strategies for enhancing proper use and compliance with medication regimens.

d. Improve culturally appropriate health care delivery.

Communication with health care professionals can be a problem for many Asian, Hispanic, and other elderly who come to the U.S. with a wide variety of educational and language skills. Often family members or friends must act as interpreters for the elderly individual in order to communicate symptoms and health care instructions between the patient and the health care provider. If the elderly individual is hospitalized or placed in a nursing home, communication becomes a critical issue in assuring appropriate health care.

Recent studies reveal that how older people are diagnosed and treated is as much a function of who they are, who is treating them, and where care is provided, as a function of the symptoms they present. Future research will focus on enhancing the quality of health care encounters to reduce health disparities associated with poor provider-patient interactions.

e. Develop strategies for information dissemination.

Because of language, educational, and cultural differences, many minority elderly individuals are not getting the information they need about healthy lifestyle behaviors. Community and religious organizations may be helpful in disseminating information. Public service advertisements can also be useful if specifically designed for foreign language newspapers, cable television, and radio. Research is needed to better understand effective strategies for communicating health messages.

f. Improve health behaviors and health promotion strategies.

Studies targeted to enhance healthy behavior in older racial and ethnic populations are a high priority. Efforts to reduce disparities through this research will include development of culturally appropriate screening tools and health care services, as well as means to enhance the likelihood of elders initiating and maintaining health promotion interventions.

Subgoal 2:

Understand Health Differences Associated with Race, Ethnicity, Gender, Environment, Socioeconomic Status, Geography, and Culture

There are many complex and interacting factors related to race, ethnicity, gender, environment, socioeconomic status, geography, place of birth and recency of immigration, and culture that can affect the health and quality of life of elderly individuals. These factors can influence work history, diet, exercise, the use of preventive health care, and the individual's role in the family and community. There are also biologic and genetic factors that can affect the course and severity of disease and disability. All of these factors must be understood in order to design interventions to improve health and quality of life.

a. Study normal aging processes in special populations.

In order to understand the course of disease and disability, it is necessary to understand "normal" aging, those processes that occur in the absence of disease. Investigators know that the prevalence of certain diseases varies among racial and ethnic populations, but very little is known about the normal processes of aging in minority populations and the similarities and differences among racial and ethnic groups, and among groups that differ on other characteristics such as geography.

b. Determine the effects of early life factors on adult health.

Aging is a lifelong process in which early life events can play an important role. Differences in nutrition, education, disease incidence and health care early in life and in fetal development can impact on disease and disability in later life. Because of the wide variety of racial, ethnic and national backgrounds in the minority elderly population, we can learn much about the impact of early life events on how well these individuals age. Research into the influence of early and mid-life experience on aging health will also improve our ability to predict health status of future cohorts of elders.

c. Develop necessary data related to health differences and causes.

Because of the complex and interactive nature of racial, ethnic, cultural, and socioeconomic variables, there is a lack of data that adequately addresses differences in health among racial and ethnic populations. More sources of data collection are needed on a national level, as well as finding ways to analyze different smaller data collection efforts. One solution could be the use of "linked data" to discover new scientific knowledge and to help in the evaluation and design of policies to deal with an aging society. Data from several sources could be linked by some common identifier and analyzed in ways not previously possible. At the same time, the use of linked data presents a complex set of challenges to maintain the confidentiality of survey respondents.

Ongoing data collection programs, such as the Current Population Survey, the National Health Survey, and the Survey of Income and Program Participation, oversample minority persons in order to provide important information on living arrangements, income, health care needs, and other topics.

Other surveys focused on specific groups include: the Hispanic Health and Nutrition Examination Survey, sponsored by the National Center for Health Statistics in 1985; the Hispanic Established Population for Epidemiologic Study of the Elderly (EPESE); the Health and Retirement Study; and the Assets and Health Dynamics of the Oldest-Old. These surveys concentrated on issues of illness and well-being. Support for these and other surveys of racial and ethnic groups will be continued and expanded in order to provide adequate data for researchers and public policy makers.

d. Promote clear and functional definitions of race, culture, and ethnicity.

Race, culture, and ethnicity can be difficult to define as the elderly population becomes more diverse. For example, black immigrants from Africa can have different languages and cultures compared to African-Americans and blacks of Caribbean ancestry. Asians can be individuals from China, Vietnam, Japan, Korea, or other nations, each with individual languages and cultures. Hispanics as a group are particularly diverse with different racial as well as cultural heritages, including American Indian, black, and white, depending on their country of origin or region of the U.S. in which they live. For research purposes it is important to have clear, consistent ways to define race, culture, and ethnicity in order to identify those factors that impact on health and allow comparison of data among different research studies.

e. Determine the relative influences of race, ethnicity, economic status, education, and work experiences in health.

Health and quality of life, particularly in later years, are attributable to many factors, some of which influence one another. To better understand risk factors for disease and preventive factors leading to good health, research is needed on separating the influence of each factor and how they work together. Longitudinal data with a life span approach are particularly important to disentangle and better understand the multitude of factors that affect health and well-being.

Subgoal 3:

Monitor Health, Economic Status, and Life Quality of Elders and Inform Policy

Socioeconomic factors including work, retirement, education, income, and wealth can have a serious impact on the health and well-being of minority individuals. 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 care insurance can determine whether an older individual enters a nursing home or stays at home to be cared for by family and friends. We still do not fully understand the interaction of financial assets and health outcomes, particularly in different racial and ethnic groups. Similarly, the role of education in improving health behaviors and health status should be better understood.

Compared to their white counterparts, minority elders as a group depend more heavily on Social Security, receive little support from private pensions, derive even less income from accumulated assets, and rely to a large extent on earnings from employment in old age. For minority elders it is of prime importance to ensure the availability of Social Security for low income individuals and to improve access to private pensions. Challenges for policy makers also include finding ways to encourage individual savings, including home ownership, and facilitate continued employment.

a. Study over time population changes and underlying causes of health and function of elders.

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 to their adult death help researchers understand the changes in health over time, and the large variations in health

across racial and ethnic populations. Research will continue to develop, maintain, and analyze longitudinal data sets.

b. Provide information useful for policy.

NIA is currently supporting the Health and Retirement Study, a nationally representative longitudinal data collection that examines retirement, economic, and family variables as they relate to health of the elderly. These studies provide data for researchers, policy analysts, and program planners who make major policy decisions affecting retirement, health insurance, savings, and economic well-being. Future studies will focus on health (physical, cognitive, and functional), dementia, economic and family resources, and care arrangements.

Recent findings of reduced disability among the elderly have become prominent in the public policy debate regarding Medicare and Social Security. Future research is needed to evaluate whether disability is being prevented or postponed, to identify contributors to disability decline, and to determine the impact of changes in health care, and to examine the economic implications of reduced rates of disability.

c. Produce 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 the different methodologies and assumptions used by scientists in calculating direct medical costs and indirect costs such as lost wages and family and informal caregiving support. All of these difficulties are compounded in minority populations due to differences in the use of formal medical care and informal family caregiving. Future projections of healthy life expectancy, longevity, and mortality depend on assumptions on how cohorts of individuals will change over time, particularly as recent immigrants are assimilated into the American "melting pot." Research will provide valuable information for projecting the need for health care services for all population groups.

d. Monitor population aging and the global burden of disease.

Population aging is not unique to the United States. As advances in sanitation, nutrition, and medical care are spread over the world, the global burden of disease has been shifting from infectious diseases to diseases of more industrialized societies, including heart disease, hypertension, diabetes, and cancer. The perspective of international studies helps increase understanding of American population aging through comparison with that of different systems.

Although many of the disparities in adult health and life expectancy across nation, county, race, occupation, and social class, are well documented, causal mechanisms are less well understood. Understanding these differences is critical for developing behavioral and public health interventions. Future research efforts will focus on developing better cross-national and sub-national databases on health outcomes, risk factors, and SES structural factors, such as societal inequality.

Goal D

Enhance Resources to Support High Quality Research

In addition to pursuing specific research opportunities, the NIA is developing the infrastructure to support future research, program management, and information dissemination. These include resources to train a skilled research workforce, providing necessary equipment and resources, and disseminating information to scientists and the public.

Subgoal 1:

Train and Attract a Diverse Workforce of New, Mid-career, and Senior Researchers Necessary for Research on Aging

The NIA is establishing and continuing programs that will result in a cadre of highly trained researchers by developing flexible training mechanisms that reflect the rapidly changing needs of science, and provide cross-disciplinary training.

It is NIA's goal to tap the talents of all groups of society. This requires that we stimulate and encourage 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. NIA intends 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.

Subgoal 2:

Develop and Sustain a Diverse NIA Workforce and a Professional Environment that Supports and Encourages Excellence

Senior NIA staff are strongly committed to worklife improvement as an ongoing process. All employees attend workshops on diversity and on prevention of sexual harassment. The NIA's Quality of Work Life Committee works with employees to identify ways to improve their working environment. Alternative work schedules, such as flexitime and flexiplace, are available to many employees.

Because the NIA operates in three locations (NIH campus, downtown Bethesda, and Baltimore), the NIA makes effective use of videoconferencing equipment and electronic sharing of files. An information resources management committee ensures smooth transitions in upgrading computer equipment and software for NIA staff. All employees have easy access to computers and use of the Internet. The NIA will continue to survey staff and provide other opportunities to improve the Institute as a workplace that respects all individuals and encourages professional development of all employees.

Subgoal 3:

Disseminate Accurate and Compelling Information to the Public, Scientific Community, and Health Care Professionals

To prevent or effectively manage chronic disease and maintain independence, patients, health care providers, and caregivers must have accurate and timely information they can use about changes that occur with aging and how to cope with health problems. The NIA's award-winning Office of Communications and Public Liaison is expanding its communications with the general public, the research community, physicians, and other health care providers to enhance dissemination of the latest advances in geriatric medicine, aging research, and related health data. All media are being used to convey these messages, which include newspaper articles, bulletins and fact sheets, professional education material, public service announcements, and videos. In addition, the NIA periodically launches national education campaigns, such as a recent one that encouraged the public to seek more information about increasingly popular "anti-aging" therapies, and another on keeping fit after 50 through exercise.

Health information and research findings are also available on the NIA web site at http://www.nih.gov/nia or can be obtained by calling 1-800-222-2225. In addition, NIA's Alzheimer's Disease Education and Referral (ADEAR) Center, an information clearinghouse, is responding to a growing need for information on AD, on its impact on individuals and families, and on research into its possible causes and cures. Professionals and members of the public can request information on AD by calling 1-800-438-4380 or by visiting the ADEAR web site, at http://www.alzheimers.org/adear. A recent addition to this web site provides information about ongoing clinical trials on AD and their recruitment status.

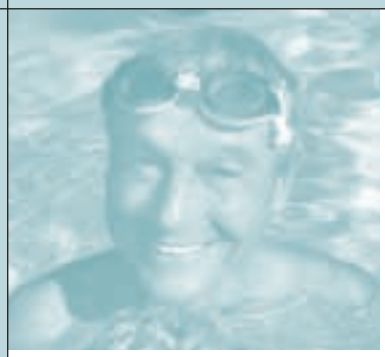
Subgoal 4:
Develop and Distribute Research Resources

Physical resources—such as animal models, chemicals, tools, and other technologies—play a critical role in research. The NIA develops and distributes these high quality resources to investigators efficiently and at reduced cost. These resources include:

- Central aging colonies of animal models, including genetically altered animals, necessary for research on aging processes and specific age-related diseases.
- Cell cultures and tissue, cell, and blood banks for basic and epidemiologic research.
- DNA resources for genetics.
- Imaging technologies for exploring the body, from the interior of the cell to organ systems.
- Computer technologies to record and analyze findings on basic biological research.

The NIA will continue to identify and evaluate opportunities for providing research resources and infrastructure development using the advice of extramural and intramural researchers.

The NIA is also evolving information technologies to assure broad access to archived data vital to researchers and policy-makers and to ensure protection of anonymity and confidentiality of participants in clinical studies. In conjunction with selected NIH institutes, the NIA plans to support research on new mathematical and informatics methodologies and on improved instrumentation and computational techniques for modeling systems changes in aging.



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