Alzheimer's Disease & Lifestyle

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This entry (a) describes the evolving definition of **Alzheimer's** disease (AD) and its prevalence; (b) summarizes evidence for nutrition, physical exercise, and other healthy lifestyle interventions that may delay onset, prevent occurrence, or slow the progression of AD and other dementias and maintain the emotional and physical health of both the person with dementia and his or her care partners; (c) identifies key lifestyle strategies for preserving brain health—both cognitive and emotional—and how they may be related to body health strategies; and (d) highlights some clinical trial results and introduces a groundbreaking multi-domain study under way in Finland and the body of evidence leading to this seminal trial.

Readers may take away confirmation of the importance of some of the things they are already doing and gain ideas and motivation to adopt brain-healthy nutrition and lifestyles.

Prevalence

The World Alzheimer Report 2010: The Global Economic Impact of Dementia, published by **Alzheimer's** Disease International, reported that around 0.5% of the world's total population live with dementia, predominantly AD, and that the total estimated worldwide costs of dementia were US$604 billion in 2010, equivalent to around 1% of the world's gross domestic product. The **Alzheimer's** Association reports that there are nearly 15 million caregivers for **Alzheimer's** and dementia patients in the United States. AD is currently the sixth leading cause of death in the United States and the one growing most rapidly (by 50% from 2000 to 2007). The growth rate of this epidemic is expected to further accelerate with the aging of the baby boomer generation, increasing personal costs to families, which provide the bulk of care, and rapidly escalating economic costs from $172 billion today to more than $1 trillion by 2050. The U.S. National **Alzheimer's** Project Act was enacted into law in January 2011 to create a coordinated national strategy to address this national public health emergency with widespread social and economic consequences.

Definition of AD and Diagnostic Criteria

AD is the most common form of dementia, causing multiple impairments in thinking and cognition, including planning and organization (executive function), attention, short-term episodic memory (especially the recording of events and experiences), and sometimes visual-spatial function. The pathological hallmarks of AD are extracellular plaques composed of a protein called beta-amyloid (also called "A-beta") and the intracellular accumulations of neurofibrillary tangles, the insoluble paired helical filaments of an abnormally phosphorylated tau protein, and a cytoskeletal protein critical to the brain cell structure. Studies suggest that the soluble forms of A-beta, not the more visible plaques, are the toxic form. The normal function of A-beta is to kill microbes, as part of the innate immune system. It is the large amount of A-beta present in AD that is abnormal. Moreover, plaques and tangles appear to be late-stage developments and may or may not reflect the initiating biological sequelae, which may

include injury, inflammation, disruptions of cell signaling pathways, oxidative stress, and disruptions in glucose and/or lipid metabolic processes.

New Criteria for Diagnosing and Redefining AD

National Institutes of Health/**Alzheimer's** Association working groups in 2010–2011 updated the criteria for diagnosing **Alzheimer's** dementia, added criteria for diagnosing mild cognitive impairment (MCI) due to underlying **Alzheimer's** pathology, and set the framework for identifying and testing biomarkers that in the near future could be used to diagnose "preclinical AD." Thus, the definition of AD has expanded beyond dementia and cognitive impairment to include a presymptomatic stage of the disease.

Biomarkers may improve the accuracy of diagnoses of both **Alzheimer's** dementia and MCI due to **Alzheimer's** pathology during life and serve as clinical trial end points. Prominent among the new biomarkers are neuroimaging (e.g., of A-beta levels, glucose processing, and the size and shape of brain structures) and measuring the presence of A-beta and tau in cerebrospinal fluid. These criteria will replace those established in 1984 as the "NINCDS-ADRDA" criteria. These criteria, developed by the National Institute of Neurological Communicative Disorders and Stroke (NINCDS) and the **Alzheimer's** Disease and Related Disorders Association (ADRDA), were universally adopted and have been in use, without modification, for more than 25 years. One of the challenges of prevention and treatment trials, both with preclinical AD and in MCI, is the inadequacy of cognitive tests to catch early changes reliably. The emergence of other outcome markers, namely brain imaging, and other biomarkers, is revolutionizing the field.

Scientists participating in the work groups formulating the new guidelines note that the updates were urgently needed for establishing the next generation of clinical trials for possible pharmaceutical and nonpharmaceutical interventions. In medical practice, the proposed changes represent refinements of existing criteria for the diagnosis of **Alzheimer's** dementia. The guidelines suggest, for example, that physicians recognize that complaints of loss of memory may not always be the first or most prominent presenting symptom. A decline in other aspects of cognition (e.g., word finding, vision/spatial issues, and impaired reasoning, judgment, and problem solving) may be the first presenting or the most prominent symptoms. Many research scientists in the field are concerned that current biomarker criteria give too much emphasis to A-beta and tau (especially A-beta) and too little to the role that oxidative stress, inflammation, vascular pathology, white matter, and other lesions or injuries may play in cognitive decline, in clinical symptoms of dementia, and in the development of abnormal levels of A-beta and tau. Ignoring a large body of evidence could hinder identifying proper treatments and preventive interventions, particularly lifestyle interventions. It is also important to guard against reductionist AD theories because what is now called "**Alzheimer's** disease" may be one or more multifactorial disorders and thus may require "multitherapies."

The evolving understanding of AD includes the recognition that individuals with a diagnoses of AD and MCI can still learn new information and acquire new habits, using a variety of preserved functions such as other forms of memory (e.g., visual, emotional, procedural). In addition, it is important to realize that while people with **Alzheimer's** may have lost many brain cells and synapses, they still retain many healthy brain cells, so it is important to work with them to maintain brain health in the hope of slowing progression, maintaining positive emotion, and improving quality of life.

Possible Causes or Etiology of AD as Related to Lifestyle

The exact causes and etiology of AD are still not fully known. As of 2011, there are still no methods of perfect diagnosis during life or ways to cure or completely prevent AD. Age remains the biggest risk factor for AD, with (lower) education levels the only other consistent risk factor across all ethnic groups. However, much has been learned in the past 30 years, lifestyles are at the heart of this new knowledge.

Research now recognizes AD as a complex chronic disease with many environmental and genetic factors, whose pathology may begin to accumulate 10 to 30 or more years before the appearance of noticeable clinical symptoms. With such a long prodromal stage, preventive interventions are needed that can be safely used for decades. While a few families have an autosomnal dominant form of AD, most individuals have what is called the "sporadic" form, without clear genetic patterns. The *APOE4* type of allele confers a dose-related risk for persons of European origin but not typically for those of African origin. While other risk-conferring genes have been identified, most scientists have found that environmental factors are probably at least as important as genetic ones. Recognition of the importance of lifestyle flows directly from the multiple studies that have shown that brain and cognitive health is dramatically affected by the rest of the body, especially the cardiovascular, glucose metabolism, and cell energy systems.

Observational and prospective studies have confirmed this logical relationship and spawned numerous animal studies to explore the relationships between particular lifestyle factors, cognition, and the mechanisms of action. For instance, physical exercise as well as many nutrients and food substances with anti-oxidant or anti-inflammatory properties have proven to lower the amount of A-beta in animal models and also lower inflammation. Some nutrients also improve neuronal cell signaling, lipid metabolism, and glucose metabolism and/or decrease oxidative stress.

This sort of evidence, together with numerous observational studies with a variety of human populations in different countries, has established that appropriate nutrition and physical activity are good candidates for helping reduce the risk of dementia, cognitive decline, and AD in humans. In 2010, gold-standard randomized clinical trials for integrated evidence-based nutrition programs had not yet been undertaken, and those for various forms of exercise had just begun. These kinds of lifestyle interventions are very difficult to get funded and then carry out, so scientists cannot yet say with certainty that the various lifestyles indicated by an array of other studies will be sufficient to delay the onset of cognitive symptoms or slow progression. However, scientists have already proven with certainty the link between nutrition, physical exercise, and certain other lifestyle factors to prevent, slow, or even reverse other related chronic diseases such as stroke, other cardiovascular diseases, diabetes, and insulin resistance. Therefore, most researchers and clinicians are ready to recommend lifestyle approaches as these offer probable additional benefits to cognitive health. Lifestyle interventions are also of keen interest since, given the multiple decades of presymptomatic development of AD-related pathology, preventive interventions need to be safe and tolerable.

A growing body of research suggests that a variety of nutritional factors, social engagement, mental stimulation, physical exercise, complex activities incorporating multiple domains, and management of stress and depression all help preserve brain health. Managing both emotional and physical stress is important because heightened cortisol levels have been connected to cognitive decline as well as to faster rates of decline in persons with **Alzheimer's** dementia. Moreover, research reports an association between cortisol levels, hippocampal shrinkage, and insulin resistance. Adequate sleep is also essential for a healthy brain, neuroplasticity, and memory. Music, art, acupuncture, T'ai Chi, meditation, and

certain other spiritual practices, as well as having a meaning and purpose in life, also appear to enhance brain health. Many of these lifestyle factors are related to neuronal plasticity and the generation of new brain cells as well as prevention of deterioration of existing brain cells.

Research indicates some common factors for both cognitive and emotional health. Intervention studies indicate the independent and synergistic efficacy of nutrition, cognitive rehabilitation, physical exercise, and various alternative medicine practices in improving cognition, mood, and quality of life of persons who already live with AD or other memory or brain disorders. The challenge is in actually making behavioral changes to adopt these protective lifestyles.

Why Lifestyle Factors Are Important to Brain Health

Epidemiological studies show that the prevalence of AD doubles every 5 years after the age of 65 (with 13% of individuals over the age of 65 having AD and about 40% over 85 years having AD). If lifestyle interventions can delay the onset of AD by 5 years, the prevalence of the disease would be halved, along with all the attendant human and financial costs.

Evidence suggests that healthy brain tissue is better able to withstand the ravages of age, genetic vulnerabilities, environmental stresses, accidents, toxins, and disease. Further, healthy lifestyles help enhance and strengthen neurons, dendrites, and other body and brain cells.

Many studies, including gold-standard clinical trials in the case of many other chronic diseases, have suggested that a healthy lifestyle, especially with regard to nutrition and exercise, may help prevent and treat most human chronic diseases. Thus, healthy lifestyles are helpful to both the person with dementia and his or her care partners, who are at extra risk of depression and illness because of caregiving.

Cardiovascular health and normal glucose metabolism contribute to brain health, while the rise in obesity and other chronic illnesses has a direct negative impact on brain health. Dozens of studies have established that each vascular risk factor adds to the risk for AD and severity of dementia.

Diabetes and prediabetes increase the risk of cognitive decline, MCI and dementia, and, according to some scientists, AD in particular. Studies using imaging techniques in adults and teenagers show that diabetes, prediabetes, or abnormally high insulin resistance as measured by glycosylated hemoglobin (HbA1c) shrinks the hippocampus, the major site for short-term memory and spatial memory, encoding of new information and experiences, as well as some aspects of emotional function. These findings should raise serious public health concerns because study results show that the hippocampi are already shrinking in obese teenagers with type 2 diabetes mellitus as well as in middle-aged nondiabetic adults with insulin resistance. Cognitive impairments in nondiabetic adults were found to be associated with the degree of insulin resistance. Related memory impairments and related white-matter changes were observed in adults with type 2 diabetes mellitus and brain-derived neurotropic factor (BDNF) levels were reduced in adults with insulin resistance.

Inflammation is believed to play a key role in the etiology of AD and has been associated with an increased risk of AD. Existing inflammation, as well as inflammatory events such as infections, surgery, or heart attacks, hastens progression in people with AD. Oxidative stress also plays a key role in AD etiology, including increasing inflammation and oxidation of brain lipids. In addition, mitochondrial dysfunction is part of AD etiology and relates to the energy systems within the brain cells.

In summary, whatever hurts the heart and blood vessels harms the brain. Problems with glucose metabolism and insulin levels also threaten the brain. The organ and disease silos are disintegrating, with increasingly similar clinical recommendations for better nutrition and exercise and for managing stress to treat or prevent a wide range of chronic diseases affecting nearly every organ in the body.

Recommended Lifestyle Approaches for Cognitive Health

Many leaders in the field of brain health believe that the evidence is already sufficient to suggest that regardless of personal risk factors, and with or without pharmacologic intervention, a healthful lifestyle is likely to reduce risk, delay onset, and slow the progression of AD and vascular dementia. Some of these researchers and clinicians conclude that the evidence suggests that it is the combination of vascular lesions (e.g., microstrokes or white-matter lesions) with **Alzheimer's** pathology that together result in symptoms of MCI and dementia. If these hypotheses are correct, then they offer another argument in favor of practicing healthy lifestyles to reduce cognitive decline.

Nutrition, physical exercise, and other lifestyle interventions work on multiple pathways to improve overall health in multiple organs with minimal or no side effects, even over many decades, which is important since scientists now believe that the pathology of AD—that is, the development of excess A-beta and abnormal phosphorylated tau—begins several decades before the appearance of cognitive symptoms.

Multiple lifestyle factors can have synergistic or additive effects. One of the most interesting trials involved the 2-year study of aged beagle dogs conducted by Carl Cotman's group at the University of California, Irvine, which showed that an enriched diet alone improved performance on a cognitive task from 25% in the control group to 67% of the experimental animals. A third group, with increased physical activity and social play, improved performance to 80%, while combining enriched diet and exercise-play interventions resulted in 100% of a fourth group of dogs being able to perform the difficult learning task.

Given the well-established connection between cardiovascular disease, insulin resistance, and diabetes and cognitive function and cognitive decline, and the evidence-based certainty that good nutrition, physical activity, and certain other lifestyle changes help treat or prevent these diseases, more and more people in the AD field have concluded that it is good clinical practice to recommend these healthy lifestyles to persons concerned about their brain health or who already have a diagnosis of MCI or dementia, including AD.

Multidomain Lifestyle Study Under Way in Finland

Many people in the field agree that the preventive intervention most likely to be effective will be multifaceted to be potent enough to delay the onset of AD or slow it down. There is one such multicenter randomized clinical trial under way in Finland, called the **Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability** (FINGER) Trial, under the leadership of Miia Kivipelto and funded by the Finnish government, the U.S. National Institutes of Health, and the national **Alzheimer's** Association (clinicaltrials.gov/ct2/show/NCT01041989). Persons between 60 and 77 years of age who are determined to be at increased risk of cognitive decline and dementia are randomized to a control group (standard health counseling at baseline) or to a preventive intervention for 2 years. The latter receive multidisciplinary treatment that includes nutritional guidance, physical exercise, cognitive training and social activity, and intensive monitoring and management of metabolic (e.g., diabetes) and

vascular risk factors. Importantly, each intervention includes a coach to guide and encourage the implementation of each lifestyle change. In addition to cognitive end points, a variety of potential biomarkers are monitored in relationship to any cognitive change, including biochemical markers of inflammation or oxidation, hormones controlling blood sugars and fats, as well as brain imaging.

Dr. Kivipelto's study reflects the combined wisdom of many leaders in the field, including the International Academy of Nutrition and Aging. The FINGER study builds on more than a decade of research, suggesting the importance of each domain of this combined program. The collective findings of some of these studies are summarized in the next section.

Selected Findings of Lifestyle Studies

Observational studies have established that each of the following lifestyle behaviors may be independently related to a lower risk of dementia: (a) nutrition, (b) physical fitness, (c) social activities and social engagement, (d) organization memberships, (e) productive (meaningful) activities, (f) mental activities (e.g., reading, word spelling/recognition, numbers, and other games), and (g) management of stress. Several researchers, using meta-analyses, have concluded that the most potent activities are complex activities that involve multiple domains, especially activities that include physical activity and social interaction as well as cognitive challenge, such as dancing and golf. Examples of activities involving 2 domains are board or card games, knitting, gardening, T'ai Chi, chi gong or yoga, and doing exercise in a group. Complex and novel activities such as learning a new language, especially sign language, traveling to new places, and playing a musical instrument, especially a new one, are also particularly recommended.

A 2010 Institute of Medicine Consensus conference and a Cochrane review of certain lifestyle interventions for preserving cognitive health concluded that there was insufficient evidence on which to base clinical recommendations. The Cochrane reviews and the Institute of Medicine, however, used very strict criteria for acceptable clinical trials, and for physical exercise, they reviewed only a few clinical trials of very small size or pilot in nature, which were underpowered. Both panels tended to be overly conservative and looking backward rather than forward in a brand new research field where rigorous clinical trials were just beginning to be designed, funded, and reviewed and where, logically, these interventions might have their biggest impact in the preclinical or MCI stage of AD, where outcome measures are still under development. Most reviews also do not integrate the combined weight of observational studies with clinical trials in animal models of AD, which are the first phase of testing some of the factors observed in human longitudinal studies and of researching mechanisms of action. Nutritional trials, especially those with integrated complex nutritional programs, are difficult to design and gain adherence to, and physical exercise programs to some extent suffer the same challenges. Published randomized controlled trials in the nutrition field as of 2011 were limited to single substances or small groups of vitamins.

Nonetheless the body of evidence is growing rapidly.

Nutrition

One well-structured prospective study published in 2010 found that persons with the highest levels of all 8 forms of vitamin E (tocopherols and tocotrienols) had half the risk of AD, whereas previous studies and intervention trials, less knowledgeable about the necessity of all forms of vitamin E in the brain and body, had looked at only α-tocopherol. This Karolinska Institutet (Sweden) study concluded that it was the combination of the 8 vitamin E forms that was important to brain health.

Various nutritional **s**tudies using animal models have shown the power of various single nutrients to lower A-beta levels, reduce oxidative stress, and improve cognitive function. Clinical trials of persons with MCI or AD have been few in number and show mixed results but some limited promise. A Swedish clinical trial of fish oil capsules using a daily dose of 1.7 mg of docosahexaenoic acid and 0.6 mg of eicosapentaenoic acid (2 long-chain omega-3 fatty acids abundant in the human brain) reported preliminary results suggesting a slowing of cognitive decline in persons with early-stage AD. A larger trial of just algae-derived docosahexaenoic acid had no effect across all AD patients. One study of 3 B vitamins (B_6, B_{12}, and folate) had no effect in persons with AD, but another using lower doses of the same 3 B vitamins improved cognition in people with MCI, but only in those with high homocysteine levels. These results suggest that while combination dietary programs may produce stronger effects on cognition than current pharmacological treatments for AD, single nutrients may be insufficient, and nutritional interventions may have more effect in MCI and very early-stage AD. Continued clinical research is needed.

Of greater interest for clinical study is combining multiple nutrients since the most recent observational studies have suggested that it is combinations of whole foods, such as in the Mediterranean or DASH (Dietary Approaches to Stop Hypertension) diets, that really make a difference. A 2006 integrative review presents evidence of how various nutrients appear to work on the multiple different pathways leading to AD and/or dementia, including inflammation, oxidative stress, glucose or insulin abnormalities, levels of A-beta and tau, cell signaling, and mitochondrial dysfunction. A recent animal study showed that a combination of whole foods–based nutrients, including vegetable, fruit, and herb and spice nutrients combined with fish oil, appears to restore mitochondrial dysfunction in triply transgenic AD mice, and a clinical trial is now under way in healthy older adults. A series of pilot studies with both mice and humans conducted by Thomas Shea and colleagues have shown preliminary success in improving short-term memory and attention in both cognitively normal adults and patients with AD, with a novel combination of vitamins and nutrients: namely, vitamin E, folic acid, vitamin B_{12}, *N*-acetyl-l-cysteine, acetyl-l-carnitine hydrochloride, and *S*-adenosylmethionine. These preliminary studies suggest an important focus for continued studies in nutrition and brain health.

Physical Activity

Most of the meta-analyses of physical activity that had less strict criteria for study inclusion than the Cochrane reviews reported consistently positive results, backing up the observational studies that had linked physical activity to reduced incidence of AD and slower rates of conversion from MCI to AD dementia. An array of intervention studies in healthy older adults, people with MCI, and people with early AD, all found evidence of decrease in the rates of cognitive decline.

Animal studies have established that physical activity increases cognitive function and identified at least 2 newer mechanisms of action beyond the known cardiovascular mechanisms: (1) decrease in levels of A-beta in the brain and (2) increased amount and rates of neurogenesis, especially in the hippocampus. Human studies have established that people who exercise more have higher levels of hippocampal BDNF, a brain chemical related to neurogenesis. Increased serum BDNF levels have been correlated with larger hippocampi and better memory performance.

Kirk I. Erickson's randomized controlled study using magnetic resonance imaging as an outcome measure established that aerobic exercise (specifically 1 year of walking 3 times a week for 40 minutes) can increase the size of critical brain structures. Consistent with the expected 1% to 2% annual

hippocampal loss in dementia-free seniors, the control group (which spent an equal amount of time stretching) lost about 1.4% volume in this brain region by the end of the 12-month trial. In contrast, the hippocampi of the walkers grew by roughly 2%. In addition, researchers found that greater elevations in serum BDNF were linked to greater gains in hippocampal volume.

The benefit of walking exercise seemed specific to the anterior part of the hippocampus (including the dentate gyrus). Similar effects did not appear in the thalamus, caudate nucleus, or posterior hippocampus. The dentate gyrus is the most metabolically active part of our brain and is involved in spatial memory, short-term memory, and new learning. Neurogenesis is most prominent in this part of the adult brain; many surmise that it is so because creation of new brain cells and dendritic connections is essential to the production of new memories.

Meditation and Spiritual Practices

Stress management and spiritual practices may also contribute to brain health. For example, a recent study using magnetic resonance imaging of the brain in live human participants reported that persons participating in an 8-week mindfulness meditation program experienced measurable increases in the hippocampus regions associated with memory, sense of self, and empathy while reducing areas of the amygdala associated with stress. Numerous studies demonstrate that other spiritual practices such as forgiveness improve emotional and mental health. By relieving stress and depression and decreasing cortisol levels, such practices may also improve cognitive health.

Cognitive Training, Cognitive Rehabilitation, and Cognitive-Kinetic Interventions

With regard to cognitive training and cognitive rehabilitation strategies to improve and preserve cognition, the evidence is particularly strong. Observational studies suggested that “use it or lose it” applies to keeping one's mind active. The groundbreaking ACTIVE randomized clinical trial study demonstrated that even short-term cognitive skills practice interventions had persistent effects in the healthy elderly. A number of later studies suggest that the most effective interventions combine modalities—for example, cognitive training with physical exercise and support groups.

Multifaceted Relationship Between Physical Activity and Cognition

In population and clinical studies, physical activity and exercise have been shown to have a positive effect on cognitive function in people of all ages. Recent studies have found that physical exercise stimulates a positive increase in executive control processes, including planning, scheduling, working memory, inhibitory processes, and multitasking. The impact of physical activity on cognitive abilities also continues through the entire lifespan. Physical exercise, for example, has been found to be a key facilitator in neurogenesis, particularly in the hippocampus as well as in other areas of the brain. In general, the rate of neurogenesis and other cognitive benefits is related to the intensity, novelty, and dose of physical activity and exercise. Both endurance (aerobic) and strength (resistance training) exercise benefit both cognitively intact and cognitively impaired individuals.

With regard to improvement in individuals with MCI and AD, substantial clinical trial evidence suggests that various cognitive rehabilitation and training strategies may help restore lost function and slow progression of cognitive decline. Different strategies appear to have more or less potent effects in only one area or in multiple areas. For example, a cognitive training strategy targeting episodic memory

benefited only episodic memory. A more holistic strategy that combined physical movements based on kinetic/cognitive theory with cognitive training benefitted areas of attention, spatial abilities, language, memory executive functions, and daily functions. Arkin's pioneering study, initially published in 1999, found a combination of simultaneous physical exercise and conversation, and language practice and word games, interspersed with volunteer activity, particularly effective.

Barriers to Adopting Lifestyle Initiatives

There are several barriers to adopting lifestyle changes, including cultural and psychological barriers. Cultural challenges include the overdependence of the American health care system, and therefore of most individuals, on pharmaceuticals and surgery, which have limited preventive roles for many chronic diseases or could be more potent if combined with lifestyle changes. Perhaps the biggest challenge for implementing these interventions as standard clinical practice is financial. Generally, lifestyle interventions are not covered by most current health insurance plans, although the concept of health promotion and prevention of illness is starting to develop. For instance, because research has established that having a "coach" or personal trainer helps individuals make lasting lifestyle changes, some private insurers will supply a free "health coach" even if the actual interventions are not reimbursed.

To promote brain health, prescribed cognitive training and physical activity may be the modalities most likely to be recognized with some incentives. Nutrition for brain health promotion is not currently covered, although individuals with diagnoses may find some limited coverage for counseling with licensed nutritionists. For families working together to provide a healthier home environment for both a patient with brain disease and his or her care partners, one possible source of funding is the National Family Caregiver Support program, which can be accessed online at www.aoa.gov/prof/aoaprog/caregiver/caregiver.asp. Individuals who have long-term care policies also may be able to gain coverage for these services. The future major solutions lie in the realm of public health, public education, public policy, and research envisioned with the 2011 passage of the National **Alzheimer's** Project Act.

—Nancy B. Emerson Lombardo

Further Readings

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