

A Review of Primary, Secondary, and Tertiary Prevention Strategies for Alzheimer's Disease

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This article explores the non-modifiable and modifiable risk factors for Alzheimer's, as well as the Alzheimer's primary prevention, secondary prevention, and tertiary prevention strategies that can be implemented. Alzheimer's is the sixth leading cause of death in the United States and the most expensive chronic disease (Alzheimer's Association, 2020). It has a detrimental physical, psychological, and financial impact on patients and caregivers (Alzheimer's Association, 2020). People can reduce their risk of developing Alzheimer's by eating a healthy diet, using hearing aids for hearing loss, engaging in regular physical activity, spending time with other people, doing mentally stimulating activities, reducing alcohol consumption, and avoiding tobacco (Livingston et al., 2020). Early screening and diagnostic tools are important because they allow people living with Alzheimer's to establish an effective care plan and to take advantage of treatments, which are most effective in the early stages of the disease (Guzman-Martinez et al., 2021). Some screening and diagnostic tools include biomarkers, scalable screening technologies, and cognitive assessments (Guzman-Martinez et al., 2021). Primary and secondary prevention strategies must address the needs of minority populations, who have a higher risk of developing Alzheimer's compared to the general population (Livingston et al., 2020). Federal public health initiatives, such as the National Alzheimer's Project Act, the Dementia Prevention Action Plan, and the Behavioral Risk Surveillance System, play an important role in Alzheimer's public health research, surveillance, and prevention strategies (Chong et al., 2021; Kelley et al., 2018).

Keywords

primary • secondary • tertiary prevention • modifiable risk factor •
non-communicable diseases (NCD) • risk reduction

Introduction

Alzheimer's is a chronic and fatal neurodegenerative disease that accounts for between 60% and 80% of all cases of dementia, a group of conditions that cause cognitive decline and impair a

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doi: 10.3998/ujph.3946

Conflicts of interest:

The author has no conflicts of interest to disclose.



person's ability to perform daily activities (Dziendzikowska & Grodzicki, 2020). It occurs due to brain tissue damage, the loss of neural connections, and the formation of tangles (twisted strands of tau protein threads) and plaques (abnormal clusters of amyloid protein fragments) in the brain (Dziendzikowska & Grodzicki, 2020). According to the CDC National Center for Health Statistics, the 2018 age-adjusted national cause-specific death rate for Alzheimer's was 30.5 per 100,000 (CDC, 2019). In 2018, there were 122,019 recorded deaths from Alzheimer's in the United States, making Alzheimer's the sixth leading cause of death and disability-adjusted life years in the United States and the fifth leading cause of death among Americans aged 65 and older (Alzheimer's Association, 2020). Although the mortality rates associated with cardiovascular disease, cerebrovascular disease, and HIV decreased between 2000 and 2018 due to medical advances, the Alzheimer's mortality rate increased by 146.2% (Alzheimer's Association, 2020). The number of Americans living with Alzheimer's is projected to increase from 5.8 million in 2020 to 13.8 million by 2050 if there is no way to prevent, slow, or treat Alzheimer's (Alzheimer's Association, 2020). In 2020, the total healthcare cost for the treatment of Alzheimer's was \$305 billion, with the cost projected to increase to over \$1 trillion by 2050, making Alzheimer's the most expensive disease (Alzheimer's Association, 2020). Population aging, which refers to the increasing proportion of people who are aged 60 years or over, contributes to the rising prevalence of Alzheimer's and the rising demand for caregivers, who face an increased risk of adverse physical and mental health outcomes (Alzheimer's Association, 2020). Public health professionals must address the escalating Alzheimer's epidemic through the implementation of primary prevention strategies, which aim to prevent the illness from developing; secondary prevention strategies, which aim to diagnose and treat the disease before the disease becomes advanced and disability becomes severe; and tertiary prevention strategies, which aim to reduce the impact of a disease by minimizing suffering and improving quality of life.

Primary Prevention

Primary prevention aims to decrease the proportion of people who develop Alzheimer's by intervening on the non-modifiable risk factors and the modifiable risk factors. Non-modifiable risk factors cannot be changed, while modifiable risk factors can be changed. The non-modifiable risk factors include female gender, older age, family history, and genetic predisposition. The modifiable risk factors can be grouped into four subdivisions: vascular (blood vessels) risk factors, lifestyle risk factors, psychosocial risk factors, and developmental risk factors. Some vascular risk factors include type 2 diabetes mellitus, heart disease, stroke, hypertension (high blood pressure), high cholesterol, obesity, and long-term exposure to air pollution (Edwards III et al., 2019).

Lifestyle risk factors include physical inactivity, which increases psychological stress and is associated with vascular and metabolic issues, poor nutrition, smoking, which increases air particulate matter and the production of plaques and tangles, and excessive alcohol consumption (Stephen et al., 2021). Obesity, hypertension, and high cholesterol and triglyceride levels have a stronger association with dementia risk in mid-life than late life (Stephen et al., 2021). A study has shown that individuals with more excess weight experience more brain cell loss and less blood flow to the brain (Dake et al., 2021). This demonstrates the importance of maintaining a healthy weight at an early age to prevent the irreversible negative effects of excess weight on the brain, especially after middle age, when the risk of developing Alzheimer's sharply increases (Dake et al., 2021). Diabetes and physical inactivity have a stronger association with dementia risk later in life (Stephen et al., 2021). People can reduce their risk of Alzheimer's and improve their overall health by making

lifestyle changes, such as eating a healthy diet, exercising regularly, achieving and maintaining a healthy weight, and treating medical conditions (Stephen et al., 2021).

Psychosocial risk factors include lower educational attainment, lower socio-economic status, poor social engagement, and low levels of intellectual stimulation (Crous-Bou et al., 2017). About 19% of Alzheimer's cases worldwide are attributable to lower educational attainment, making lower educational attainment the most important modifiable risk factor for Alzheimer's as well as the earliest (Crous-Bou et al., 2017).

Developmental risk factors include sleep deprivation, depression, epilepsy, traumatic brain injury, hearing loss, which leads to social isolation, a loss of cognitive stimulation, brain atrophy (a loss of connections between neurons), oral diseases, which trigger an inflammatory response, infections, chronic work-related stress, and early childhood stress (Crous-Bou et al., 2017). Stress triggers neuroinflammation (an inflammatory response in the brain) and oxidative stress (physiological stress that occurs due to the release of harmful chemicals called free radicals) (Crous-Bou et al., 2017). In a study of 2,000 individuals aged 71–78 years, work-related stress was associated with a 55% increased risk of Alzheimer's (Galvin, 2017).

Modifiable risk factors cause about a third of Alzheimer's cases worldwide, demonstrating that risk factor reduction can aid in Alzheimer's prevention (Crous-Bou et al., 2017). One lifestyle risk factor reduction strategy is regular physical activity due to its increase of neuroplasticity (the brain's ability to change and adapt due to new knowledge and experiences) and high-density lipoprotein (HDL) cholesterol, as well as its reduction of inflammation and plaque formation (Crous-Bou et al., 2017). In the Hisayama Study, higher participation in daily physical activity was associated with a 50% reduction in risk of Alzheimer's (Zhang et al., 2021). Aerobic exercise improves oral fluency and executive function through its protective effects on neuronal health and hippocampus volume (Zhang et al., 2021). A prospective study found that a one-year aerobic exercise training program improved memory ability and blood flow to the brain (Zhang et al., 2021).

Another lifestyle risk factor reduction strategy is adherence to the MIND Diet for Neurodegenerative Delay, a combination of the Mediterranean diet and the Dietary Approaches to Stop Hypertension (DASH) diet (Janoutova et al., 2020). The Mediterranean diet includes fruits, vegetables, fish, legumes, whole-grain cereals, low-fat dairy products, monounsaturated fatty acids, little red meat, and moderate amounts of red wine and caffeine (Janoutova et al., 2020). The DASH diet includes low-fat dairy products, fruits, vegetables, small amounts of sweets and meats, and a limited amount of sodium, total fat, saturated fat, and cholesterol (Janoutova et al., 2020). A longitudinal study including 960 participants of the Memory and Aging Project found that the MIND Diet was associated with a slower rate of cognitive decline and that it improved executive function, memory, and visual construct (Grande et al., 2020). Evidence also supports the long-term use of omega-3 supplements and antioxidant vitamins, such as carotene, vitamin C, or vitamin E, in cognitively healthy mid- and late-life subjects to decrease the likelihood of developing Alzheimer's (Guzman-Martinez et al., 2021). Vascular risk factor reduction strategies should focus on intervening in the risk factors for cardiovascular disease and Alzheimer's, such as diabetes, hypertension, and high cholesterol. Some strategies include early screening and intervention of vascular risks, better blood pressure monitoring, resin therapy for cholesterol lowering, and the maintenance of optimal cardiovascular health. Other strategies include folic acid supplementation to lower homocysteine levels, the management of blood glucose, blood pressure, blood lipid, and weight, and pharmaceutical uses like metformin and other anti-diabetic drugs, antihypertensives, and catheter ablation and oral anticoagulants. An example of a cardiovascular risk reduction intervention is

the Systolic Hypertension in Europe (Syst-Eur) trial, a randomized controlled trial that included 2,418 non-demented adults aged 60 and older with systolic hypertension. The researchers found that an active hypertension treatment of enalapril, hydrochlorothiazide, nitrendipine, or a combination of these reduced the incidence of dementia by 50% (Hsu & Marshall, 2017). Psychosocial risk factor reduction strategies include individual education, meditation and yoga to improve mindfulness (the human ability to be fully present and aware of one's thoughts, feelings, sensations, and surrounding environment) and to reduce stress, frequent social engagement, and participation in cognitive activities, such as solving crossword puzzles, reading, playing games, and learning different languages (Langa, 2018). These strategies increase cognitive reserve, the brain's ability to maintain normal cognitive performance for a longer period and to resist age-related neuropathological changes, including progressive neuronal loss and cellular damage (Langa, 2018). An example of a cognitive-related intervention in the United States is the Advanced Cognitive Training for Independent and Vital Elderly, (ACTIVE) study, a randomized controlled trial that included more than 2,800 cognitively healthy adults older than 65 years who attended ten group sessions during a six-week period, where they received training in reasoning, memory, or processing speed (Crous-Bou et al., 2017). After the ten-year follow-up, the researchers found that the adults who received cognitive interventions exhibited better cognitive functioning and less functional decline in daily living activities compared with the control group (Crous-Bou et al., 2017). The long-term effects on cognition play an integral role in public health prevention because they decrease the overall burden of Alzheimer's (Crous-Bou et al., 2017). Another study showed that living in a neighborhood with institutional resources, such as recreational facilities, community centers, and libraries, was associated with better cognitive function after controlling for individual risk factors for cognitive decline (Langa, 2018). In the World-Wide Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGERS) trial, a multidomain lifestyle intervention that combined cognitive training, dietary counseling (high-protein snacks, glycemic control, MIND Diet), social interaction, management of vascular and metabolic risk factors, and exercise incorporating strength and aerobic training boosted cognitive scores among healthy elderly people who were at risk for dementia, regardless of socioeconomic or sociodemographic factors (Hodes et al., 2018).

A 2017 cross-sectional study validated the multiple findings of observational studies regarding the association between cognitive performance and hypertension, obesity, vascular risk factors, diabetes mellitus, and depression (Galvin, 2017). Dementia shares many common lifestyle risk factors and protective factors with other non-communicable diseases (NCDs), which are illnesses that cannot be transmitted from one person to another and have multiple causes (Stephen et al., 2021). Some NCDs, such as diabetes and obesity, are also risk factors for dementia (Stephen et al., 2021). Therefore, the most cost-effective and feasible dementia preventative interventions will target multiple factors for multiple NCDs (Stephen et al., 2021). Primary prevention policies for dementia can incorporate existing programs and campaigns related to other NCDs, including population health promotion that emphasizes tobacco cessation, alcohol use disorder rehabilitation, weight management, increased physical activity, and adequate nutrition, and specific strategies that address socially active lifestyles, cognitive-stimulating activities, and childhood or formal education (Stephen et al., 2021). The 2017–2025 WHO Global Action Plan on the public health response to dementia states that dementia preventative measures should converge with mental health, existing NCDs, and aging efforts worldwide (Stephen et al., 2021). Public health professionals, researchers, and policymakers can establish evidence-based multidomain interventions at the individual,

community, and population level that target dementia specific risk factors when treating NCDs (Stephen et al., 2021).

The 2020 Lancet Commission on Dementia Prevention describes population-based interventions and individually targeted interventions for Alzheimer's primary prevention. Population-based interventions include improving access to childhood education, providing high-quality, affordable health and social care services, and decreasing the risk of brain trauma by requiring helmets and seatbelts in occupational and transport settings. Other interventions include developing policies that promote social, cognitive, and physical activity across the life course, developing social public health policies that decrease hypertension risk in the population, establishing international and national policies to decrease population exposure to air pollution, examining the risks for hearing loss throughout the life course and reducing excessive noise exposure, and strengthening international and national efforts to decrease exposure to smoking and other addictive substances in childhood, adolescence, and adulthood. Individually targeted interventions include preventing head trauma where an individual is at high risk, treating hypertension and aiming for a mean systolic blood pressure level of less than 130 mm Hg in midlife, and participating in smoking cessation programs. Other interventions include sustaining mid-life and late-life physical activity, refraining from drinking 21 or more units of alcohol per week, using hearing aids for hearing loss, and making lifestyle changes (Livingston et al., 2020).

Preventive interventions must address racial and ethnic disparities in Alzheimer's risk that occur due to the following socioeconomic factors: low household income, low education attainment, and low literacy level (Livingston et al., 2020). Socially disadvantaged populations, including Asian, Black, and ethnic minority groups, have the highest risk of developing Alzheimer's (Livingston et al., 2020). They will reap the greatest benefits from preventative interventions that improve access to education, decrease excessive noise exposure, and decrease hypertension, obesity, and diabetes rates by increasing the availability of nutritious foods and by establishing more physical activity-supportive built environments (Livingston et al., 2020). Other populations that have an increased Alzheimer's risk include older adults, Hispanics, American Indians and Alaska Natives, and individuals with developmental disabilities (Olivari et al., 2020). The use of linguistically, culturally, and age-appropriate public health prevention strategies is necessary to improve access to and the quality of care, which will decrease disparities among these populations (Olivari et al., 2020). Partnering with organizations that focus on these populations can increase intervention effectiveness and impact on disparities (Olivari et al., 2020). Accurate and timely data and community involvement play a crucial role in the development of prevention strategies (Olivari et al., 2020).

Secondary Prevention

Secondary prevention aims to target the pre-symptomatic or preclinical stage and prevent the development of Alzheimer's symptoms through the appropriate use of screening and early diagnostic tools, including biomarkers, scalable screening technologies, and cognitive assessments, followed by prompt treatment (McDade et al., 2021). The five stages of Alzheimer's screening, diagnosis, and care in secondary prevention are as follows: the detection of the disease through screening, the assessment of individuals for cognitive impairment or Alzheimer's pathology, the differentiation of Alzheimer's from other causes of cognitive impairment using blood work analysis for

thyroid hormone or vitamin B12 deficiencies, computed tomography (CT) or structural imaging with magnetic resonance imaging (MRI) for the detection of head injury, stroke, or tumors, the diagnosis of Alzheimer's using biomarkers, brain imaging, mental status tests, and physical and neurological exams, and the immediate treatment and monitoring of patients, which is the responsibility of a patient-centered dementia care team (Galvin et al., 2021). During the preclinical stage, the neuropathological changes indicative of Alzheimer's are present decades prior to the emergence of clinical symptoms that result in an Alzheimer's diagnosis (Guzman-Martinez et al., 2021).

The preclinical stage is the most opportune time for Alzheimer's screening, diagnosis, and treatment because the screening and identification of individuals with preclinical Alzheimer's precede therapies that slow or prevent the onset of Alzheimer's more effectively during the preclinical phase than the clinical phase, when significant neurodegeneration has already occurred (Guzman-Martinez et al., 2021). The first phase of Alzheimer's disease is the pre-clinical or the pre-symptomatic stage, which is characterized by neuropathological changes in the hippocampus and mild memory loss (Breijyeh & Karaman, 2020). These changes occur without clinical symptoms and with no functional impairment in daily living activities (Breijyeh & Karaman, 2020). The second phase is the mild or early stage, which is characterized by slight impairment in daily living activities, disorientation of time and place, mood changes, depression, and a loss of memory and concentration (Breijyeh & Karaman, 2020). The third phase is the moderate stage, which is characterized by neuropathological changes in cerebral cortex regions, increased memory loss, a loss of impulse control, difficulty in reading, writing, and speaking, and difficulty recognizing family and friends (Breijyeh & Karaman, 2020). The fourth phase is the severe or late stage, which is characterized by the buildup of tangles and plaques, a spread of the disease to the entire cortex region, an inability to recognize family and friends, an inability to move, and difficulties in urination and swallowing (Breijyeh & Karaman, 2020). One of the primary causes of death for Alzheimer's patients is pneumonia, which occurs when impaired swallowing allows food to enter the lungs, causing an infection (Breijyeh & Karaman, 2020). Other common causes of death include malnutrition, falls, dehydrations, and other infections (Breijyeh & Karaman, 2020).

Treatments that delay the clinical onset of dementia in individuals with preclinical Alzheimer's will increase longevity, decrease lifetime risk, and decrease the number of Americans ages 65 and older living with dementia by 2.2 million by 2040 (Zissimopoulos et al., 2018). Due to the lack of disease-modifying (ability to slow the progression of a disease by targeting the underlying cause) treatments for symptomatic individuals, it is important to prevent neurodegeneration, cognitive decline, and dementia (Guzman-Martinez et al., 2021). Screening programs during the preclinical phase will improve the quality of life and chances of survival for millions of people worldwide, decrease the global economic impact of Alzheimer's, and allow researchers to design trials for individuals with preclinical Alzheimer's (Guzman-Martinez et al., 2021). Although positron emission tomography (PET) imaging of amyloid and the measurement of cerebrospinal fluid levels of tau and amyloid proteins increase diagnostic confidence, they are expensive and invasive evaluation methods that carry the risk of over-diagnosis (ten Kate et al., 2018). Despite the predictive value of screening for neuropsychological symptoms in individuals without clinical symptoms, biomarkers that are sensitive to pathological change can improve prognostic accuracy (ten Kate et al., 2018). The National Institute on Aging-Alzheimer's Association (NIA-AA) and the International Working Group (IWG) suggest the use of reliable, inexpensive, and non-invasive biomarkers to classify preclinical Alzheimer's as the disease stage in which amyloid plaques, tangles, and hallmarks of neurodegeneration are evident, even in the absence of clinical symptoms (ten Kate et al., 2018).

Early-stage biomarkers should predict the risk and timing of cognitive decline in a cost-effective, non-invasive, and reliable manner (ten Kate et al., 2018). Clinical trials in individuals without Alzheimer's would benefit from biomarkers that can detect pathological changes over time and in response to treatment, monitor treatment effects and reflect disease progression, and be reproducible and reliable in a multicenter setting (ten Kate et al., 2018). Neuroimaging techniques enable researchers to detect and quantify functional, structural, and molecular brain changes that are characteristic of Alzheimer's preclinical and clinical stages (ten Kate et al., 2018). Imaging and fluid biomarkers that can identify individuals with preclinical Alzheimer's include amyloid and tau protein buildup, a low amount of glucose production, and neurodegeneration as measured by MRI (McDade et al., 2020). Blood-based biomarkers measure specific proteins associated with the neuropathological hallmarks of Alzheimer's and can screen large populations due to their lower costs, reduced invasiveness, and increased acceptance by patients (Ojakaar & Koychev, 2021). Digital biomarkers and scalable screening technologies monitor functional, sensory, cognitive, and behavioral changes in individuals at risk for Alzheimer's, decrease the burden on the healthcare system, and allow patients to monitor their own risks throughout their lives (Ojakaar & Koychev, 2021). Examples of digital biomarkers include wearable devices, smartphones, and infrared sensors, which obtain information about health-related aspects of daily life, such as sleeping, walking, and taking medications (Ojakaar & Koychev, 2021). Monitoring programs can use biomarkers to identify individuals who would benefit from targeted interventions of specific risk factors and disease-modifying treatments using amyloid clearance therapies, which are in the development process (Ojakaar & Koychev, 2021).

An early and accurate Alzheimer's diagnosis facilitates the development of an effective care plan, which requires coordination between the patient, family members, caregivers, social services, payers, specialists, and healthcare professionals, and non-pharmacological interventions that mitigate cognitive decline, decrease caregiver burden, and decrease healthcare costs by about \$7 trillion (Galvin et al., 2021). Examples of non-pharmacological interventions include psychological treatment, cognitive simulation, and lifestyle changes, all of which decrease severity and rate of disease progression (Galvin et al., 2021). An early diagnosis also benefits individuals by decreasing anxiety and improving social support (Galvin et al., 2021). However, in the current healthcare system, individuals suspected of having Alzheimer's often receive continuous referrals and wait years for a diagnosis and treatment (Dickens & Ramaesh, 2020). Since cognitive decline is gradual, clinical manifestations of Alzheimer's are not apparent to patients and caregivers until later stages of the disease (Dickens & Ramaesh, 2020).

An ideal cognitive screening test should maintain adequate specificity (a test's ability to identify a negative result for an individual who does not have the disease) and sensitivity (a test's ability to identify a positive result for an individual who has the disease) (Iatraki et al., 2017). It should also be brief, easily administered and scored, and uninfluenced by sociodemographic factors (Iatraki et al., 2017). The Mini-Mental State Examination (MMSE) is the most commonly used screening tool for cognitive impairment (Iatraki et al., 2017). It is an 11-question test that assesses orientation, attention, memory, language and visual-spatial skills, comprehension, motor skills, and problem-solving skills (Iatraki et al., 2017). It asks individuals to repeat a sequence of words, identify an object, name three unrelated objects, and name the city, state, and country they are in (Iatraki et al., 2017). It has demonstrated reliability and validity in neurologic, psychiatric, and geriatric populations (Iatraki et al., 2017). However, it is not the best option for primary care because it is time-consuming and requires special training for administration and scoring (Iatraki et al., 2017).

Cognitive screening tools that are better options for cognitive screening of elderly rural populations in medical and primary care settings are the Test Your Memory Test (TYM) and the General Practitioner Assessment of Cognition (GPCog Patient Scale) (Iatraki et al., 2017). The TYM assesses specific aspects of memory-related cognitive function, takes 5–10 minutes to complete with little supervision, and is easily scored by non-medical professionals (Iatraki et al., 2017). The GPCog-Patient Scale consists of a one-minute memory test in which a physician has a short conversation about memory with the patient and an informant interview with the caregiver about the patient's cognitive function (Iatraki et al., 2017). This screening tool demonstrates a need for more detailed cognitive assessments (Iatraki et al., 2017). The "Mini-Cog test" requires patients to memorize a short list of words, draw a clock face, and repeat the memorized words (Dickens & Ramaesh, 2020). The Montreal Cognitive Assessment (MOCA) requires a 15-minute planned interview and evaluates the following cognitive functions: concentration, memory, language, conceptual thinking, calculations, orientation, visuospatial skills, attention, and executive functions (Dickens & Ramaesh, 2020). Physicians should use cognition tools in conjunction with normal screening blood tests, discussions with carers and relatives, and an investigation of the patient's medical history (Dickens & Ramaesh, 2020).

In 1984, the Alzheimer's Disease and Related Disorders Association (ADRDA) and the National Institute for Neurological and Communicative Disorders and Stroke (NINCDS) collaborated to establish the diagnostic criteria for Alzheimer's, which was then updated in 2011. These criteria comprise probable Alzheimer's disease, possible Alzheimer's disease, and definite Alzheimer's disease. Probable Alzheimer's disease can be diagnosed by dementia that is confirmed by progressive memory loss, impaired daily life activity, agnosia (a loss of perception), aphasia (a loss of the ability to understand and express language), and apraxia (a motor skills disorder that makes it difficult to speak). These symptoms begin from age 40 to 90 years in the absence of brain diseases. Possible Alzheimer's disease is applied in the absence of neurological or psychiatric disorders that are not the main cause of dementia. Definite Alzheimer's disease is confirmed by a histopathological evaluation obtained from an autopsy or biopsy (Breijyeh & Karaman, 2020).

There are four public health priorities to improve screening and diagnosis in secondary prevention: increasing awareness of the clinical value of early detection in the population by educating people about Alzheimer's and its treatment options, educating healthcare professionals about the clinical features of early-stage Alzheimer's and the most effective ways to communicate with Alzheimer's patients, non-dementia specialist healthcare professionals to take appropriate action early, and establishing a step-by-step process that will stratify patient risk and help healthcare professionals decide whether to conduct further cognitive assessments or make subsequent referrals to dementia specialists (Galvin et al., 2021). Alzheimer's education programs should train healthcare professionals to discuss cognitive symptoms with their patients, take discussion of memory concerns from the patient or family members seriously, use dementia screening instruments with high validity and reliability for the detection of dementia, and acknowledge the predictive value of subjective concerns about cognitive problems (Galvin et al., 2021). The collection of data on normal and abnormal cognitive aging will help healthcare professionals identify risk factors and early clinical symptoms of Alzheimer's (Galvin et al., 2021). Community education will empower patients to take charge of their cognitive health and destigmatize Alzheimer's by dispelling the notion that a person with Alzheimer's is sick or elderly (Galvin et al., 2021). It will help people learn how to identify Alzheimer's stigma, become more comfortable talking about stigma, interact with people and families affected by Alzheimer's disease, and avoid making negative judgments

that are untrue about people with Alzheimer's (Herrmann et al., 2018; Johnson et al., 2015). Eliminating the stigma associated with Alzheimer's is important because stigma can prevent individuals and families from receiving a diagnosis, benefitting from treatments, developing a support system, participating in research, and planning for future medical, long-term, and end-of-life care (CDC, 2015). The 2015 Gerontological Society of America's Kickstart, Assess, Evaluate, Refer (KAER) model provides educational resources and clinical tools that guide primary care teams in the initiation of conversations with patients about cognitive health, the detection and diagnosis of dementia, and the provision of community-based resources for individuals (Gerontological Society of America, 2015).

Tertiary Prevention

Tertiary prevention aims to target the clinical stage and the disability stage when primary prevention and secondary prevention are unsuccessful (Ojakaar & Koychev, 2021). The goal of tertiary prevention is to increase life expectancy and quality of life, improve well-being, prevent complications of Alzheimer's, and limit disability and immobility (Ojakaar & Koychev, 2021). Tertiary prevention interventions are most effective when they are implemented in the earliest stages of Alzheimer's (Ojakaar & Koychev, 2021). Researchers established a multidisciplinary rehabilitation program to examine the effects of cognitive rehabilitation, cognitive stimulation, physical training, computer-assisted cognitive training, art therapy, and occupational therapy on cognitive decline (Ojakaar & Koychev, 2021). They found that the program decreased depressive symptoms and improved cognition and quality of life in patients with mild Alzheimer's in the intervention arm, but not in patients with moderate Alzheimer's (Ojakaar & Koychev, 2021). This underscores the importance of screening and early diagnosis in secondary prevention.

Successful Alzheimer's management requires open physician, caregiver, and patient communication, behavioral approaches, caregiver support, and pharmacological interventions (Papageorgiou & Yiannopoulou, 2020). Open physician, caregiver, and patient communication allows physicians to identify symptoms, evaluate and diagnose, and provide guidance (Papageorgiou & Yiannopoulou, 2020). Behavioral approaches include established routines, communicative strategies such as using simple language, providing enjoyable activities, calm and respectful interactions, saying no only if safety is concerned, consistency and simplification of the environment, timely planning for legal and medical decisions and needs, cognitive behavioral therapy, exercise therapy, light therapy, and music therapy (Papageorgiou & Yiannopoulou, 2020). Caregiver support interventions include planned short rest periods for the caregiver and psychoeducation, which teaches caregivers how to prepare for the effects of Alzheimer's on cognition, function, and behavior, how to avoid situations that can worsen symptoms or endanger the health of a person with Alzheimer's, and how to develop support networks (Papageorgiou & Yiannopoulou, 2020). Caregiver support interventions are an important part of tertiary prevention because the increasing Alzheimer's morbidity and mortality rates as well as the increasing number of patients dying at home indicate that there is an increasing number of Alzheimer's caregivers (Taylor et al., 2017). Education, case management, and respite care reduce the physical, emotional, and financial burden of caregiving and improve the quality of care for Alzheimer's patients (Taylor et al., 2017).

Although current pharmacological interventions cannot stop or reverse Alzheimer's disease progression, they can temporarily improve symptoms (Papageorgiou & Yiannopoulou, 2020). There are

two categories of FDA-approved medications: the acetylcholinesterase inhibitors (AChEIs) donepezil, galantamine, rivastigmine, and the N-methyl-D-aspartate (NMDA) antagonist memantine (Papageorgiou & Yiannopoulou, 2020). AChEIs prevent the breakdown of acetylcholine, a neurotransmitter that activates muscles and assists with processing speed, short-term memory, and learning (Papageorgiou & Yiannopoulou, 2020). Alzheimer's patients have lower acetylcholine levels due to the degeneration of cholinergic neurons, which are nerve cells that use acetylcholine (Papageorgiou & Yiannopoulou, 2020). AChEIs improve communication between nerve cells and decrease cognitive decline during the first year of treatment (Papageorgiou & Yiannopoulou, 2020). In randomized placebo-controlled trials up to 52 weeks duration, all three AChEIs slowed or stabilized cognitive decline and improved cognition and activities of daily living (Papageorgiou & Yiannopoulou, 2020). Temporary discontinuation of these drugs leads to rapid decline and a higher likelihood of nursing home placement (Papageorgiou & Yiannopoulou, 2020). The FDA-approved rivastigmine and donepezil for mild, moderate, and severe Alzheimer's, and galantamine for mild and moderate Alzheimer's (Papageorgiou & Yiannopoulou, 2020). NMDA antagonist receptors work by blocking the action of NMDA, a glutamate receptor and neurotransmitter that helps regulate breathing, learning, memory formation, and neuroplasticity (Papageorgiou & Yiannopoulou, 2020). Alzheimer's patients have an excess amount of glutamate, which damages and kills healthy brain cells (Haque & Levey, 2019). Memantine can treat moderate and severe Alzheimer's as monotherapy or in combination with an AChEI (Haque & Levey, 2019). It is associated with better cognitive, neuropsychiatric, and behavioral symptoms, and improved ability to perform activities of daily living (Haque & Levey, 2019). Other medications include antipsychotics and antidepressants, which can treat behavioral, psychiatric, and cognitive symptoms (Papageorgiou & Yiannopoulou, 2020). Selective serotonin reuptake inhibitors, such as citalopram, escitalopram, and sertraline, can treat anxiety and depression (Papageorgiou & Yiannopoulou, 2020). The development of a personalized Alzheimer's treatment regimen factors in the patient's comorbidities, disease stage, and frequency and intensity of cognitive, behavioral, and psychological symptoms (Papageorgiou & Yiannopoulou, 2020).

According to the 2020 report of the Lancet Commission, tertiary prevention interventions that benefit Alzheimer's patients include physical activity, cognitive training, psychosocial management of treatment and care, discussions with a psychiatrist or neurologist, and telemedicine (Livingston et al., 2020). Other interventions include the provision of holistic post-diagnostic care for patients and caregivers that addresses cognitive, psychological, medical, environmental, social, and cultural needs, and the detection and management of physical problems, such as sensory impairment, diabetes, pain, falls, and incontinence (Livingston et al., 2020). Caregivers and healthcare professionals must monitor hydration, sleep, and nutrition status; manage vascular risk factors (diabetes, hypertension, hyperlipidemia); treat deficiencies in vitamin D, vitamin B12, and folate; treat thyroid and electrolyte disorders; and treat systemic diseases that can influence cognition, such as pain, constipation, and infections (Papageorgiou & Yiannopoulou, 2020). Individuals with dementia have higher rates of cerebrovascular disease, anxiety and depression, pneumonia, incontinence, electrolyte disturbance, skin ulcers, diabetes, and Parkinson's disease compared to the general older population (Livingston et al., 2020). Since multimorbidity accelerates functional decline and lowers the quality of life for people with dementia and their caregivers, the management of comorbidities is a critical public health intervention at the tertiary level (Livingston et al., 2020).

Federal Public Health Initiatives

The National Health and Medical Research Council National Institute for Dementia Research (NNIDR) Dementia Prevention Special Interest Group has established the Dementia Prevention Action Plan, which incorporates public health preventive strategies at the primary, secondary, and tertiary prevention levels. The first strategy is to create public health and clinical practice guidelines for dementia prevention across the life course in primary care and other settings. Some dementia prevention interventions include secondary prevention in memory clinics for those at high risk, the development of occupational and environmental policy to decrease hearing loss, air pollution, and traumatic brain injury, and the prioritization of early life educational attainment. The second strategy is to train primary care providers to lead dementia prevention efforts. The Medicare Benefits Schedule should increase focus on dementia prevention through the creation of new Medicare Benefits Schedule item numbers and modification of existing items, such as the health check for individuals aged 45–49 years who are at risk of developing chronic diseases. Private health insurers can broaden the scope of preventive health services to address dementia risk factors and reward individuals who participate with greater rebates for health services or lower insurance premiums. The third strategy is to fund research for evidence-based interventions for modifiable risk factors for dementia. The fourth strategy is to establish health promotion programs using findings from dementia risk reduction and implementation research. The fourth strategy is to improve the diversity of dementia prevention public health campaigns. The fifth strategy is to organize a coordinated dementia prevention effort that includes government, nongovernmental organizations, industry, education, research, all levels of the health sector, policymakers, and the community. The sixth strategy is to coordinate public health messaging on dementia risk factors that relate to chronic diseases, such as cardiovascular disease and diabetes (Chong et al., 2021).

In 2011, President Barack Obama signed into law the National Alzheimer's Project Act (NAPA), which has funded Alzheimer's research and has instituted many large clinical trials to study Alzheimer's interventions (Olivari et al., 2020). NAPA aims to prevent and treat Alzheimer's by 2025 through the establishment of infrastructure for effective research practices, the translation of preventive practices into community health settings, and the cooperation with large organizations worldwide to enhance targeting efforts (Olivari et al., 2020). Public health strategies include utilizing timely population-based data to set priorities, implementing public education campaigns, and improving core competencies for healthcare professionals (Olivari et al., 2020). In 2005, the CDC and the Alzheimer's Association partnered to establish the Healthy Brain Initiative to combat the Alzheimer's public health crisis (Kelley et al., 2018). The most recent publication, *Healthy Brain Initiative: The Public Health Road Map for State and National Partnerships, 2018–2023*, described 25 actions that state and local public health agencies can take to support cognitive health (Kelley et al., 2018). The CDC also established the Behavioral Risk Factor Surveillance System, which provides annual data on caregiving surveillance and cognitive decline, and the Healthy Aging Data Portal, which provides public health professionals and policymakers with access to state, regional, and national health-related data on older adults (Kelley et al., 2018). Public health professionals can use evidence-based information and surveillance data at the local, state, and federal levels from this report to help Americans maintain optimal cognitive health (Kelley et al., 2018).

Conclusion

Despite being historically perceived as merely an aging or medical issue, Alzheimer's is a serious public health epidemic with a tremendous and rapidly increasing global, national, and regional burden that takes a physical, emotional, and economic toll on patients, caregivers, families, the healthcare system, the government, and society (Healthy People, 2020, 2021). The number of people living with Alzheimer's will continue to exponentially increase each year and double by 2030 due to longer life expectancies and population aging (Healthy People, 2020, 2021). To address the Alzheimer's public health crisis, public health professionals must collaborate with healthcare professionals, policymakers, and non-governmental organizations on the development of a multidisciplinary approach that consists of primary prevention strategies based on the identification of modifiable and non-modifiable risk factors and protective factors, secondary prevention strategies based on screening, early detection, cognitive screening assessments, and intervention at the presymptomatic stage, tertiary prevention strategies based on rehabilitation, caregiver support, pharmacologic interventions, cognitive training, the provision of geriatric care services, opportunities for social interactions, the management of comorbidities, and the mitigation of the effects of the coronavirus pandemic on Alzheimer's patients, and federal public health initiatives (Healthy People, 2020, 2021). The inclusion of Alzheimer's in Healthy People 2020 for the first time highlights the public health threat that Alzheimer's poses to the United States (Healthy People, 2020, 2021). According to Healthy People 2020, important public health interventions include increasing the availability and quality of diagnostic tools, promoting cognitive decline risk reduction, strengthening public health surveillance, and reducing the number of people with undiagnosed dementia (Healthy People, 2020, 2021). Other interventions include decreasing the severity of cognitive, behavioral, and neuropsychiatric symptoms through medical management, promoting healthy behaviors, increasing public awareness of Alzheimer's, reducing preventable hospitalizations, and supporting family caregivers with legal, social, and behavioral resources (Healthy People, 2020, 2021). During the next decade, the public health sector must make progress in improving the early diagnosis and management of Alzheimer's, researching the effect of genetic, environmental, lifestyle factors on Alzheimer's risk across the life course, and implementing effective interventions to delay or prevent the onset of Alzheimer's (Healthy People, 2020, 2021). These objectives can reduce Alzheimer's morbidity and mortality rates, improve the quality of life for Alzheimer's patients and their caregivers, and optimize cognitive health outcomes for all Americans.

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