Chapter 18
Preventing What's Preventable in Dementia

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18.1 Introduction

The high frequency of television and online ads for supplements, brain fitness gadgets, and other products that purportedly preserve cognitive functioning suggests that older adults are increasingly concerned about declines in memory as they age. However, given cultural stigma around memory loss, relatively few individuals discuss these worries with their primary care physicians (PCPs) or behavioral care providers (BCPs). A study conducted by the Center for Disease Control (CDC) of almost 96,000 individuals aged 45 years or older revealed that approximately 13% indicated they experienced confusion or memory loss in the previous year, but only 23% of those with such concerns raised the issues with a medical professional (National Center for Chronic Disease Prevention and Health Promotion, 2012).

Despite having limited information to guide their choices of strategies with the greatest benefits to promote cognitive wellness, many older Americans have embarked on their own experimentation by engaging in exercise, diet, meditation, participating in lifelong-learning programs, playing brain performance computer games, or taking over-the-counter supplements, with the hope that such behaviors can, in sum, prevent dementia (Hartman-Stein & LaRue, 2011). Others have a fatalistic view that nothing can be done to prevent Alzheimer's or have no interest in the

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topic, so they eat highly processed fast food more than vegetables and fruits, limit their reading to online posts, and/or engage in minimal exercise.

It is not merely members of the lay public who question whether lifestyle makes a difference—health providers are often dubious as well. We believe PCPs and BCPs can help patients protect and maintain their brain health, regardless of their level of belief, by advising, supporting, and teaching based on the current state of knowledge.

In 2019 the Alzheimer's Association surveyed about 1000 primary care physicians, finding that:

- Over 80% acknowledge they are on the front lines of diagnosing and providing care for Alzheimer's disease (AD) and other dementias.
- Over half of PCPs receive questions related to dementia from their patients age 65 and older or their family members every few days or more.
- More than one-quarter (27%) report being only sometimes or never comfortable answering patient questions about dementia (Alzheimer's Association, 2020a, b).

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18.2 Incidence, Prevalence, and Etiologies of Dementia

The word dementia is an umbrella term referring to a wide range of medical conditions caused by brain changes. AD is a progressive neurodegenerative disorder characterized by early symptoms of difficulty recalling recent conversations, names, or events, being repetitive, having trouble following a complex train of thought, having difficulty following conversations, or withdrawing from work and social activities. Later symptoms include impairment in communicating, disorientation, confusion, poor judgment, declines in problem-solving and the ability to perform activities of daily life (Alzheimer's Association, 2020a, b; Gerontological Society of America, 2020). AD accounts for approximately 60–80% of all cases of dementia, affecting approximately 20% of individuals 80 years of age and older (Alzheimer's Association, 2020a, b; McKhann et al., 2011).

The leading hypothesis as to its etiology is that the intercellular accumulation of the protein fragment, beta-amyloid, triggers a cascade of extracellular amyloid accumulation that then cause tau proteins—structures providing stability within neurons—to twist into intracellular tangles, leading to widespread neuronal death (Selkoe & Hardy, 2016). In individuals with rare genetic mutations, levels of beta-amyloid may begin upwards of 20 years before symptoms occur (Quiroz et al., 2018). Other brain changes in AD include chronic inflammation and atrophy due to cell loss that may begin over a decade before becoming symptomatic. Microglia clear proteins and debris from dying cells, and inflammation may set in when microglia are unable to clear the debris adequately (Alzheimer's Association, 2020a, b).

However, mixed dementias—i.e., cases that encompass not only the classic hallmarks of plaques and tangles but also overlapping pathologies like vascular lesions, alpha-synuclein (the protein making up Lewy bodies), and TDP-43, a nuclear protein in common subtypes of frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS), appear to be more common than recognized as more than 50% of people with dementia have pathologic changes indicating more than one cause of dementia. The likelihood of having mixed dementia increases with age (Alzheimer's Disease Facts and Figures, 2020a; Winblad et al., 2016; Yu et al., 2020). Recent studies of TDP-43 suggest that more complex brain pathology leading to cognitive decline in late-life may be independent of beta-amyloid accumulation (Kawas et al., 2015; Wilson et al., 2013). Such findings indicate that treating only pathways that converge on beta-amyloid, as is the focus of current drug development, may leave untreated a significant proportion of the associated conditions in the AD phenotype that are not related to plaque and tangle pathology (e.g., vascular damage).

In a book that sparked controversy at the time, *The Myth of Alzheimer's: What you aren't being told about today's most dreaded diagnosis,* the authors dismissed the promise of a pharmaceutical panacea for AD as a cultural myth promoted by powerful drug companies (Whitehouse & George, 2008). In 2016 the pharmaceutical company, Merck, announced it was halting the late-stage trial of verubecestat, a BACE inhibitor that controlled an enzyme involved in the forming of amyloid plaques, abnormal protein clusters in the brain that have been suspected as a main cause of Alzheimer's disease. The drug did not reduce cognitive or functional decline in patients with mild-to-moderate AD and was associated with treatment-related side effects such as rash, falls and injuries, sleep disturbance, suicidal ideation, and weight loss (Egan et al., 2018).

In late 2016 the drug company, Eli Lilly, ended its clinical trial of the drug, solanezumab, after research subjects demonstrated no improvement compared to placebo. The failure of drugs in the family of BACE inhibitors developed to reduce amyloid added to doubts to the viability of the amyloid theory of AD (Hartman-Stein, 2017). Moreover, as of winter 2020, the FDA had declined to approve Biogen's drug aducanumab—a monoclonal antibody acting on different molecules than solanezumab. Researchers have made the case that given the ongoing failures of drug development, the best investment of research dollars is for prevention and improved interventions (George & Whitehouse, 2021; Whitehouse & George, 2008).

A recent major study in *JAMA Internal Medicine* published findings showing the incidence rate of dementia for people over age 65 has been dropping in the United States, from 11.6% in 2000 to 8.8% in 2012 (Langa et al., 2017). While *overall* numbers of people affected by dementia continue to rise—as one would expect, given the growing population of aging individuals who are living longer—there has been a general *decline* in both dementia incidence (the number of people diagnosed per year) and prevalence (the number of people diagnosed relative to the total number of people in the population) over the past four decades (Gao et al., 2019; Wu et al., 2017). Indeed, emerging research published in *Neurology* suggests that due to decreasing risk, older Americans' chances of developing dementia in 2021 is 13% lower than it was in 2011 (George & Whitehouse, 2021; Wolters et al., 2020). It is

likely that improved vascular health at the population level, along with significantly reduced smoking rates, increased access to primary, secondary, and tertiary education, and the removal of toxins like lead from gasoline in the late twentieth century have combined to provide a more favorable milieu for the brain health of current cohorts of elders (George & Whitehouse, 2021; Livingston et al., 2020).

Despite the fact that dementia risk is dropping, the following current figures from the Alzheimer's Association (2020a, b) are sobering:

- 5.4 million Americans and 50 million people worldwide live with dementia.
- AD is the sixth leading cause of death in the United States and fifth leading cause for those age 65 and older.
- People with AD live an average of 8–10 years and as many as 20 years from onset.

18.2.1 Sequelae of Covid-19

What is not yet known is the impact of Covid-19 on the incidence of dementia and AD. In early 2021 with guidance from the World Health Organization (WHO), the Alzheimer's Association, in conjunction with 30 countries, has formed a consortium to study more than 22 million Covid-19 cases to evaluate the impact of the virus on the risk of later life cognitive decline and AD (de Erausquin et al., 2021).

18.3 Common Categories of Dementia/Diagnostic Criteria

According to the Gerontological Society of America (GSA) (2020), the most commonly used categories of dementia coded in PC settings include: dementia from AD with early onset (<age 65); dementia from AD with late onset (age 65 or older); dementia from AD, unspecified; vascular dementia with or without behavioral disturbance; dementia in other diseases classified elsewhere with or without behavioral disturbance; unspecified dementia with or without behavioral disturbance; Pick's disease (described below); other frontotemporal dementia; dementia with Lewy bodies; mild cognitive impairment; and corticobasal degeneration.

Symptoms that may indicate dementia and trigger more in-depth evaluation are deficits from baseline skills in learning and retaining new information, problem-solving, reasoning, spatial ability, orientation, word finding, following conversations, and behavioral changes such as passivity, irritability, suspicion, and misinterpreting visual or auditory stimuli (GSA, 2020).

According to the American Heart Association (AHA)/American Stroke Association (ASA), probable vascular dementia is indicated when there is cognitive impairment and imaging evidence of cerebrovascular disease, a clear temporal relationship between a vascular event (e.g., clinical stroke) and onset of cognitive

deficits, and a clear relationship in the severity and pattern of cognitive impairment with the presence of diffuse, subcortical cerebrovascular pathology (Gorelick et al., 2011).

Pick's disease is a rare type of age-related dementia that affects the frontal lobes of the brain and causes speech problems like aphasia, behavior difficulties, and eventually death. It had been used interchangeably with frontotemporal dementia (FTD) but is now considered to be one of three very specific causes of FTD. Pick's disease is not usually associated with memory loss in its early stages (https://www.alzheimers.net).

FTD may occur in those 65 and older but most people with the disorder develop it a younger age (Alzheimer's Association, 2020a, b). The three subtypes are behavioral variant (bvFTD), semantic variant of primary progressive aphasia (svPPA), and non-fluent variant of primary progressive aphasia (nfvPPA). Neuropsychiatric symptoms are prominent in bvFTD.

Lewy body dementias include two related disorders, dementia with Lewy bodies (DLB) and dementia secondary to Parkinson's disease. Essential for the diagnosis is fluctuating cognition with variations in alertness, recurrent visual hallucinations, rapid eye movement sleep behavior disorder before signs of cognitive decline, and one or more features of Parkinsonism. In the early stages, there may be no memory impairment but deficits in attention, executive functioning, and visual-spatial ability may be present (Gerontological Society of America, 2020; Yamada et al., 2020).

The criteria for mild cognitive impairment (MCI) due to AD include concern regarding cognition that reflects a change reported by the patient, informant, or clinician indicating observed evidence of decline over time. In addition, there must be evidence of impairment in one or more cognitive domains, including memory while independence in functioning capacity is preserved (Albert et al., 2011). Traditionally, the MCI label has been given to patients who present with a memory complaint and some changes in intellectual function as determined by neuropsychological testing but who have relatively little impairment in activities of daily living.

A range of sub-classifications, however, has recently emerged that implies different stages of MCI: pre-MCI, early MCI, and late MCI. However, conversion rates of MCI to dementia vary significantly, and some studies observe that well over a quarter of people labeled with MCI do not progress to AD (Pandya et al., 2017) and between 14% and 41% of individuals with MCI have reverted back to "normal" cognitive functioning (Ganguli et al., 2004). Naturally, this has raised questions about the accuracy, usefulness, and ethical soundness of a label that is supposed to represent a clinical precursor to AD.

18.4 When Screening Is Warranted

The idea of widespread dementia screening in PC is debatable. Galvin et al. (2020) argue screening increases self-efficacy and improves patient-centered outcomes for lifestyle changes. However, both the Lancet Commission and the US Preventive

Services Task Force (USPSTF) conclude the evidence is lacking to support widespread pre-symptomatic screening in everyday practice (Livingston et al., 2020; US Preventive Services Task Force, 2020).

There are substantial ethical concerns about the push for early diagnosis through memory screenings. As mentioned earlier, the greatest controversy surrounds the heterogeneity observed in "pre-disease" categories such as MCI, the vagueness of its diagnostic criteria, and a lack of specific ability to predict the "disease" trajectory. If an aging person has some memory loss, but their activities of daily living are not affected, what is the value in screening them and clinically labeling them with MCI? When does the forgetfulness we may all be touched by as our brains age cross the line to "disease"? Should a clinical diagnosis be freely given by the physician or should it also require a subjective complaint from the patient or family members? This concern speaks to a broader societal question about how much power physicians (and the pharmaceutical industry) should have in defining and dictating the terms of how individuals experience disease, which can have such devastating effects in the lives of their loved ones. Indeed, it is important to remember that while markets and shareholder profits may be enlarged by diagnostic schemes that extend labels like MCI to more people, ultimately human beings with fragile, finite lives and bonds must bear the biopsychosocial consequences of disease labels (George & Whitehouse, 2021).

Screening and an accurate diagnosis are important for patients with notable impairment and/or personal or family members' concerns about their loved one's functioning. An excellent free resource for PC that can be downloaded online is *The GSA KAER Toolkit for Primary Care Teams: Supporting conversations about brain health, timely detection of cognitive impairment, and accurate diagnosis of dementia* (www.geron.org/programs-services/brain-health-cognitive-impairment-and-dementia).

The toolkit suggests that the PCP or BCP bring up the topic of brain health for educational purposes at any PC visit or as part of an annual wellness visit for every person age 65 or older. Examples of questions about concerns or change in functioning include: "Are you worried about your memory? Have you noticed any changes that concern you?" If the patient or family member raise concerns regarding memory loss or other signs of cognitive decline, then more formal screening administered by the BCP or a medical assistant who has had adequate training can administer a brief formal assessment. Front desk staff may observe behaviors such as confusion about appointments, repetition of stories or questions, or deferring to family members for basic information. In a PC setting with a large patient volume, creating an atmosphere that encourages all staff to give input will enhance patient care.

Even if no concerns arise, the BCP can use a brain health conversation to provide information about the connections between brain and heart health, medications that may affect memory, dietary patterns, and lifestyle habits that impact the brain. *Communicating with older adults: An evidence-based review of what really works* is a free resource developed by the Gerontological Society of America (GSA)

containing tips for optimizing interactions between healthcare providers and older adults (Gerontological Society of America, 2012).

If screening is warranted, using a validated, brief cognitive test is advisable. The KAER toolkit recommends the Mini-Cog©, Clock Drawing test, Montreal Cognitive Assessment (MoCA), or the Saint Louis University Mental Status (SLUMS) exam. All take 10 min or less to administer. Another short test of mental status used extensively in clinical and research settings is the Mini-Mental State Exam (MMSE) developed at Johns Hopkins Medical Center (Folstein et al., 1975).

Informant questionnaires to obtain collateral information are also part of a valid screening process. The KAER toolkit lists the Ascertain Dementia eight-item Questionnaire, the Informant-based Behavioral Pathology in Alzheimer's Disease rating scale, and the Short Form of the Informant Questionnaire on Cognitive Decline in the Elderly (GSA, 2020).

Screening is not typically adequate to make a diagnosis. In most cases, we recommend when screening shows impairment, PCPs and BCPs partner with specialists such as geriatricians, geropsychologists, neurologists, neuropsychologists, or nurse practitioners with geropsychiatric expertise.

When there are symptoms of cognitive impairment, the reversible physiological causes of cognitive decline should be ruled out first through appropriate laboratory tests (e.g., thyroid or vitamin B12 deficiency). The GSA toolkit contains e-resources for PCPs and BCPs with suggestions of how to talk to patients and families about a diagnosis of dementia.

18.5 Risk Factors and Recommendations

Evidence is growing that dementia can be prevented or delayed and that healthy lifestyle changes may be beneficial for older at-risk individuals even in the presence of APOE-related genetic susceptibility to dementia (Solomon et al., 2018). Two separate international groups of scientists published their meta-analyses of research reports of both observational prospective studies (OPSs) and randomized control trials (RCTs) (Livingston et al., 2017, 2020; Yu et al., 2020). The team led by Yu et al. (2020) identified 19 modifiable factors and the Lancet Commission on dementia (Livingston et al., 2020), described 12 modifiable risk factors, accounting for 40% of dementia worldwide. To offer guidance for dementia prevention across the life span, we have summarized these evidence-based suggestions PCPs and BCPs can provide to patients from these studies.

- **Receive as much education as possible in early life and engage in cognitive activities throughout life**. As noted earlier, dementia rates are falling over the last decade in part due to increased access to education in the mid-twentieth century. Examples of life-long cognitive activities include reading, playing chess, solving problems, learning a second language, playing music, traveling to novel areas, writing narratives, and doing art work.

Additional corroborating evidence comes from a population-based longitudinal observational study in the oldest-old begun in 2003 of 587 people age 90 or older who had no signs of dementia when the study began. Participation in activities with a strong mental component, i.e., reading and church/synagogue attendance, was correlated with reduced risk of dementia as the participants aged beyond 90 (Paganini-Hill et al., 2016).

No single specific activity such as solving crossword puzzles or playing computerized games appears to protect against cognitive decline, although domain-specific training of focal skills may improve. For example, doing crossword puzzles on a regular basis improves crossword puzzle skills (Livingston et al., 2020).

The *Lancet* Commission (Livingston et al., 2020) noted that older retirement age is correlated with lower dementia risk for more cognitively demanding jobs. The take-home message is if a person's work is meaningful and mentally challenging, it may be advisable not to retire early.

Cognitive reserve theory, a concept that began in the late 1980s, may explain these findings. Cognitive reserve refers to the brain's structural and functional ability to build resilience against neurological damage, tolerate more brain pathology before signs of dementia occur, or draw upon multiple pathways in undertaking cognitive tasks. In a post-mortem analysis of 137 patients, some subjects who showed no signs of AD upon autopsy had high degrees of pathology but higher brain weights and a greater concentration of neurons compared to age-matched controls. The theory is that these individuals had cognitive reserve that served as a protective factor against cellular deterioration (Katzman et al., 1988; Whitehouse & George, 2008). Other OPS of religious orders show similar findings (Snowdon, 2003).

- **Encourage use of hearing aids for hearing deficits and protect ears from excessive noise exposure.** Cognitive reserve theory may explain that those who cannot hear properly may over time experience exponentially less cognitive stimulation.
- **Manage weight and BMI**. Given links between weight, vascular health, and brain health, it is beneficial to encourage BMI for individuals <65 to be between 18.5 and 24.9. Moreover, BMI ought to be maintained <30 in mid-life and beyond, but adults over 65 should not be overly thin and, if losing weight, they should be monitored.
- **Control vascular factors**. Ideally, systolic blood pressure should be kept to 130 mm Hg or less from age 40 on. Patients should be encouraged to maintain good condition of cerebral vessels via lifestyle or medications to avoid any cardiovascular disease. Individuals with history of stroke or cerebral micro-bleeding should be monitored for cognitive changes. Instances of atrial fibrillation should be managed and patients should be encouraged not to smoke and to avoid second hand smoke. Diet/exercise should be used to avoid diabetes while monitoring blood sugar levels for those with diabetes. Homocysteine levels should be monitored as high levels can contribute to arterial damage and result in blood clots. Vitamin B and/or folic acid can treat this condition.

- **Limit alcohol use with no more than 21 units weekly, i.e., no more than three drinks of any kind per day**. The 2020–2025 Dietary Guidelines for Americans differ somewhat in their recommendations, suggesting that for those who choose to drink, intake should be limited to one drink or less per day for women and two drinks or less in a day for men (US Department of Health and Human Services and US Department of Agriculture, 2020). While the deleterious effects of excess alcohol consumption are well-established, some mild-to-moderate alcohol consumption may be protective in reducing inflammation (Barve et al. 2017).
  Engage in physical exercise. Individuals 65 and older should be encouraged to engage in regular physical exercise and an active lifestyle by movement in daily activities such as taking stairs and engaging in hobbies such as yoga, dancing, and gardening. Both the Lancet Commission (Livingston et al., 2020) and Yu et al. (2020) suggest older adults maintain good cardiovascular condition, but there is no strong evidence as to what types of exercise, duration, frequency, or intensity are needed to achieve optimal cognitive functioning. Public health recommendations indicate older adults should be encouraged to engage in an active lifestyle that incorporates movement in everyday activities, and if possible, purposeful exercise with moderate to vigorous exertion including strength and aerobic training (Global Council on Brain Health, 2016).
  Limit or avoid head trauma. Traumatic brain injuries (TBI)—bumps, blows, or jolts to the head or neck area—can cause acute damage to the brain, and even multiple mild injuries can contribute to greater cumulative risk throughout life. Wearing helmets for contact sports and bike riding and wearing safety belts at all times should be encouraged for all ages, and caution should be taken to avoid falls (the leading cause of TBI), especially in later life stages when balance may be compromised.
- **Ensure consistent patterns of sleep**. Sleep increasingly appears to help the brain's glymphatic system remove metabolic waste that has accrued through the day. Sleep deprivation can downregulate the glymphatic system, leading to the buildup of toxic cellular waste products that can damage and impair the brain over time (Fultz et al., 2019). Several lines of evidence suggest that sleep disorders may contribute to cognitive decline and may be a promising target for prevention (Xu et al., 2020). According to the *Lancet* Commission, there is no evidence that medication for sleep is effective, but rather considerable evidence suggests its harm (Livingston et al., 2020). Thus, behavioral strategies to improve sleep are of great importance.

  BCPs can counsel patient individually or in groups on sleep hygiene including relaxing strategies before bedtime and following middle-of-the-night awakenings. Yu et al. (2020) recommended individuals get sufficient and good quality sleep but do not give specific suggestions for optimal amounts. Current health guidelines recommend at least 7 h of sleep per night, but a longitudinal observational study of 613 individuals found no differences in cognitive measures or structural measures of the brain between groups that reported 5.4, 6.2, 7, and 7.9 h of sleep over 5 points in time over 28 years. This study calls for replication,

and if results are the same, it will challenge current sleep guidelines (Zitser et al., 2020).

- **Limit stress and treat depression**. Stress and depression are well-established lifespan risk factors for dementia (Livingston et al., 2017). Thus, patients should be guided toward individually tailored stress reduction strategies, e.g., practicing mindfulness-based stress reduction (Kaszniak, 2011), increasing frequency of pleasant and meaningful activities (Richards et al., 2016), and/or dealing with root causes of stress or depression. In the only RCT comparing behavioral activation to supportive therapy for preventing dementia in patients with amnestic MCI, those in the behavioral activation group had a decreased 2-year incidence of risk of memory decline (Rovner et al., 2018).

  Maintaining frequent social contacts improves mood. Research has shown that maintaining social networks is protective, and, conversely, that the effects of loneliness, isolation, and disconnection are risks comparable to smoking up to 15 cigarettes a day, obesity, physical inactivity, and air pollution (Holt-Lunstad, 2017). Social service agencies can provide regular phone or computer-based contact with isolated, vulnerable older adults. Referral to local area agencies on aging or community mental health centers is strongly recommended in such cases.
- **Medications.** Two interventions not recommended are estrogen replacement therapy and acetylcholinesterase inhibitors (Yu et al., 2020). De-prescribing anticholinergic medications is advisable. In an observational cohort study with 350 adults with follow-up of 3.2 years, anticholinergic medications were found to increase the transition from normal cognition to MCI in community-dwelling older adults without dementia (Campbell et al., 2018). Anti-hypertensive medication is the only known preventive medicine against cognitive decline (Livingston et al., 2020).

Dietary Supplements

Many dietary supplements have been promoted for maintaining or improving cognitive function. Apoaequorin, a calcium-binding protein originally derived from jelly fish, is contained in the widely advertised supplement, Prevagen. Although several animal studies on its safety have been published, human data on its efficacy are limited to published abstracts or studies posted on the company's website (Hume, 2015).

Despite the widespread advertisements for supplements, the Lancet Commission (Livingston et al., 2020) does not recommend additional vitamins, oils, or mixed dietary supplements as a means of preventing dementia because testing in trials lacked beneficial effects. However, in the 90+ study, a population-based longitudinal study, supplemental vitamin C intake around age 90 reduced risk of dementia in the oldest-old (Paganini-Hill et al., 2016).

18.6 Nutrition in the Prevention of Cognitive Decline

Because several risk factors are related to what we eat, we have included detailed information regarding research on nutrition. RCTs are somewhat limited in regard to neuroprotection. For many years, chronic disease prevention consisted of reducing intake of certain dietary components, such as saturated fat and sodium. The current major focus is on overall eating patterns and intake of bioactive compounds. Increasingly, research is demonstrating that the microbiome—the massive ecosystem of bacteria, viruses, and fungi that live in our intestinal tract and can be weakened or strengthened by the quality of our diets (and other lifestyle factors)—may have a role to play in modulating neural, immune/inflammatory, endocrine, and metabolic pathways that affect our aging brains across the lifespan. Plant-based, Mediterranean-like diets have been shown to be most beneficial to the health of our microbiota (Izaskun et al., 2018).

Some evidence suggests that individual food bioactive components protect cognitive health, including vitamins B and D, anti-oxidant vitamins, medium chain triglycerides, and long chain omega-3 fatty acids sourced from oily fish (Jennings et al., 2020). However, risks for stroke and cardiovascular disease have been the primary targets for preventing cognitive impairment (Gorelick et al., 2017), and cardioprotective diets have been extensively investigated (Appel et al., 1997; Harsha et al., 1999; Ornish, 1998; Saneei et al., 2014; Shah et al., 2017; Wright et al., 2017).

Hypertension is recognized as a modifiable risk factor for dementia (Livingston et al., 2020; Yu et al., 2020). The Dietary Approaches to Stop Hypertension (DASH) diet, formulated in the 1990s, remain a cornerstone of treatment for high blood pressure and has resulted in beneficial effects in many RCTs (Appel et al., 1997; Harsha et al., 1999).

Plant foods (e.g., vegetables, fruits, whole grains, legumes) form the foundation of all the heart healthy plans as well as fresh, whole, unprocessed foods, i.e., foods in a form as close to the original as possible.

In our experience, the general public has limited understanding as to what processed food entails, so we suggest explaining it to patients. Physical processing can be simply washing, peeling, heating, or chilling or more complex, such as milling or fermentation of grains. Some definitions refer to the number of additives that can maintain or improve food safety, freshness, taste, texture or appearance. Ultra-processed food (UPF) tends to be high in calories but generally contributes little fiber and few nutrients. While minimally processed foods are easily recognized, three classification systems rate the degree of processing in foods (Bleiweiss-Sande et al., 2019). Examples from the University of North Carolina (UNC) system give the following examples of highly processed, multi-ingredient, industrially formed mixtures that are no longer recognizable in their plant/animal source: soda, fruit drinks, lunch meat, breads made with refined flour, pastries, ice cream, processed cheese, and candy. Consuming less of these is recommended in all of the brain-heart healthy diets described below.

The role of animal products and added fats is what varies most in the recommendations of the plans. Herbs and spices are encouraged in many of these diets for flavor and for the bioactive compounds they contain. Turmeric, or Indian saffron, found in Asian curries, some pickles and yellow mustard, is promising in dementia prevention (Desai et al., 2011), but without evidence in RCTs. Curcumin, the active ingredient in turmeric, has anti-inflammatory properties (Aggarwal & Sung, 2009).

The Mediterranean diet, recommended by the World Health Organization to reduce risk of cognitive decline and described in *The Blue Zones* (Buettner, 2015), is not truly a single diet but a plant-based eating pattern, incorporating vegetables, fruits, whole grains, nuts, and oils, especially olive oil. Lifestyle habits other than diet, such as social networks, daily rituals, sense of purpose, are discussed in *The Blue* Zones and also in the low-fat Ornish plan (1998), Ornish & Ornish (2019).

The programs devised by Ornish (1998) and Esselstyn (2007) differ notably from Mediterranean-type diets in that fat, even from plant sources, is severely restricted. While RCTs are more limited, retrospective and OPS have consistently shown plant-based diets to be associated with lower risk of cognitive decline, dementia, the pathology of Alzheimer's syndrome, as well as cardiovascular disease and diabetes.

The Dash Diet, studied in RCTs to lower blood pressure, includes lean meats, poultry, fish, and eggs and allows olive and other vegetable oils (Saneei et al., 2014). The MIND Diet which combines aspects of the DASH and Mediterranean diet specifies minimum servings of green leafy vegetables (6 plus/week), berries (twice/week), nuts (5times/week), whole grains (3/day), fish (once/week), beans (4 times/week), and poultry (at least twice/week). Butter and margarine, cheese, red meat, fried foods, and sweets are limited. In a prospective study of over 900 participants over 4.5 years, moderate adherence to the MIND diet decreased AD risk (Morris et al., 2015).

In a small RCT over a six-month period, the Nordic diet improved lipid profiles and had a beneficial effect on low-grade inflammation (Uusitupa et al., 2013). This diet features beans, peas, roots, and tubers (carrots, parsnips, beets, potatoes). Fish and seafood are eaten often while red meats and animal fats are limited. Followers are encouraged to eat higher-quality meat but less of it. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER), a 2-year long, multi-domain RCT, used "the healthy Nordic diet" similar to the Mediterranean diet (Ngandu et al., 2015).

Very low-fat plans that discourage consuming any oil, Ornish (1990, 1998) and Esselstyn (2007), emphasize eating green leafy vegetables and encourage generous amounts of all vegetables. Esselstyn's plan is vegan, while Ornish allows egg whites and nonfat dairy products. Both include whole grains and protein sources such as tofu, tempeh, beans, and legumes and limited use of nuts and seeds.

In the BROAD study, a small RCT that used a whole food plant-based (WFPB) diet, participants had improved BMI and cholesterol and reduced other risk factors, which were largely maintained at 12 months (Wright et al., 2017). The EVADE CAD trial (Shah et al., 2017), also a WFPB vegan diet, assessed multiple cardiovascular risk factors in patients with coronary artery disease treated with

guideline-directed medical therapy. The vegan diet reduced systemic inflammation (measured by high sensitivity C-reactive protein).

An eight-year longitudinal study of over 22,000 people in southern Italy, age 43–67, indicated that those who ate the most UPF had the highest risk for cardiovascular disease, even among those who adhered to the Mediterranean diet, linking the consumption of junk foods to poor health outcomes (Bonaccio et al., 2020).

The table below lists diets recommended for heart and potentially brain health, the unique features of each diet, including what to avoid.

Major features of diets for heart/brain health

	Meat, fish, and poultry	Dairy	Eggs	Fat	Alcohol	Herbs and spices	Other
Vegetables, fruits, and whole grains are the foundation of all diets listed							
Mediterranean—type: 25–35% of calories from fat							
Mediterranean				Olive oil	Red wine		
DASH	Lean meats, poultry, and fish; includes eggs	Low fat and nonfat	Allowed	Limit sat fat and tropical oils	Limit	Encouraged	Nut, seeds, legumes 4–5 x/ week Limit sugars
MIND	Fish emphasis	Low-fat and nonfat	Allowed	Olive oil	Limit to 1 glass/day	Include liberally	Emphasis on berries and leafy greens
Nordic	Fish emphasis	Low-fat and nonfat	Free range	Rapeseed oil	Limited	Encouraged	Fish readily available in region
Very low fat: supplementation might be required							
Ornish	None	Nonfat milk, yogurt, cheese	Whites	4 g/day; 1 low fat serving of nuts/seeds encouraged	No more than 1 glass of wine, 1 beer or 1 shot of whiskey/ day	Low salt; herbs and spices for flavor	Eliminate all added oils and avocados; reduce white flour, white rice. Limit sugar
Esselstyn	None	None	None	No animal fat; no oils	Any kind in moderation	Include liberally	Avocados OK if low lipids

The US Department of Health and Human Services (HHS) and the US Department of Agriculture publish evidence-based food and beverage recommendations to promote health, prevent disease, and help people reach and maintain healthy weight. The *2020–2025 Dietary Guidelines for Americans* that provides advice for people from birth to older adulthood are a valuable resource for primary care (US Dept. of HHS & US Department of Agriculture, 2020).

Primary care providers have opportunities to directly educate patients. A first step is to have early conversations about nutrition to educate about risk factors, including targeted questions such as: How many meals/week (breakfast, lunch, and dinner) do you obtain from restaurants? When you eat at home, do you cook "from scratch" or use prepared meals or packaged products? Are there days when you do not eat any vegetables or fruits?

What are you able and willing to do to begin to eat a healthier diet?

Step 2: Provide a list of hand-outs and electronic resources that include information about healthy eating and foods to avoid, including examples of UPF. If feasible, offer individual or group programs, possibly through tele-health, to support positive, individualized, tailored changes in dietary habits (Rosenberg, Mangialasche, Ngandu, Solomon, & Kivipelto, 2020).

Step 3: Refer patients to a Registered Dietitian/Nutritionist who wants to pursue Medical Nutrition Therapy (MNT) in greater depth for optimal health and especially patients with comorbidities, such as diabetes, obesity, or those with food intolerances or allergies.

18.7 Multi-Modal Interventions

Because of the complex and multi-factorial nature of AD and other dementias, interventions that target multiple risk factors are being studied across the world. The FINGER study is the first large (1200 older adults at-risk for dementia), long-term (2 year) RCT to demonstrate positive results for improved cognition in the group that received multi-domain interventions that included exercise, diet, cognitive training, and management of metabolic and vascular risk factors (www.alzheimersprevention.org; Ngandu et al., 2015).

The FINGER lifestyle intervention is being tested in 25 other countries, including the United States, known as the World Wide FINGERS (WW-FINGERS) initiative launched in 2017 to reduce risk in different geographical, cultural, and economic settings (Kivipelto et al., 2020.) The next generation of multi-domain prevention trials have begun with a trial of 2724 computer-literate, cognitively intact participants over age 65 from Finland, France, and the Netherlands. The intervention group received support to manage cardiovascular risk factors over the Internet from a remote lifestyle coach. Data analyses have not yet been released, but if results are positive, self-management strategies may be feasible to reach a large worldwide population (Rosenberg et al., 2020).

Payment for Prevention and Management of Chronic Conditions

Educating and counseling patients about their diet, stress level, and exercise take time, and administrators of healthcare systems using fee-for-service payment may scoff at the lack of practicality of PCPs or BCPs engaging in these practices unless they can be reimbursed for such services. Once, yearly wellness visits under Medicare plans are hardly adequate from a patient care perspective, but things are changing. In 2011 a paradigm-shift in reimbursement occurred in which Medicare began to pay for 72 h of the Ornish Lifestyle Medicine under Intensive Cardiac Rehabilitation. This program includes supervised exercise by an exercise physiologist, stress management led by a certified yoga/meditation teacher, support groups run by a psychologist or social worker, and 1 h of a group meal and lecture by a dietitian (Ornish & Ornish, 2019).

In 2017 Medicare began payment in PC for chronic care management for patients with two or more chronic conditions, such as diabetes, hypertension, cardiovascular disease, depression, and risk factors for dementia. The coding for these services is beyond the scope of this chapter, but we recommend billing personnel in PC to determine the feasibility of using the chronic care management codes. BCPs can be reimbursed under the health and behavior assessment and intervention codes that are intended to improve the management of patients with medical conditions who do not have psychiatric disorders.

These changes in Medicare payment are a start; however, these sets of billing codes systems under Medicare are largely for managing chronic conditions rather than prevention. Only when prevention services are widely reimbursed or population-based approaches to integrated healthcare become common-place will prevention services become the norm in PC.

18.8 Cutting Edge of Dementia Prevention

Since the early 1970s, the neuroscientific evidence for the cognitive, emotional, and health-related benefits of meditative practices has increased exponentially from a handful of studies to over 6800 in the last few years (Goleman & Davidson, 2017). Kaszniak (2011) described a promising study of mindfulness-based stress reduction (MBSR) to improve well-being and attention task performance among caregivers of persons with dementia.

Small scale studies sponsored through the Alzheimer's Research and Prevention Foundation (ARPF) suggests that a yoga meditative practice known as Kirtan Kriya (KK) done 12 min a day is an important component of a lifestyle program for stress reduction to prevent AD along with following a plant-based diet and engaging in regular physical and mental exercise (Khalsa, 2014; Wirth et al., 2014). However, no large-scale RCTs were found to date using this meditative practice comparing it to other stress reduction techniques. In 2020 Ornish and his colleagues at the Preventive Medicine Research Institute began the first RCT to determine if the progression of

early-stage AD may be slowed, stopped, or reversed. The components are a plant-based diet, moderate exercise, psychosocial support, and meditation.

The fourth pillar promoted by the ARPF, largely absent from RCTs, promotes personal growth, improvement of relationships, and finding purpose in life, similar elements included in Dean Ornish's plan for managing chronic illness (Ornish & Ornish, 2019).

18.9 Lessons Learned/Implementation

With patients who have concerns about their memory, we hope the days are over of doing nothing more than watchful waiting or reflexively prescribing drugs like donepezil, without suggesting sustainable lifestyle changes. We suggest that patients' fears about age-related memory loss are acknowledged with reassurance that there are steps that can, in many circumstances, delay or prevent further decline, even in individuals at high risk due to their genetics.

- Given a patient's age and individual risk factors, a one-size-fits-all preventive approach is not reasonable nor likely to be effective. We recommend designing a plan, with the patient's input, that reduces the individual's risk profile, beginning with two or three lifestyle changes the patient is open to trying.
- There is also no one-size-fits-all recommendation for exercising cognitive skills. A challenge that is new and stretches one's skills is good, but if the activity is too hard, people may become discouraged and stop. Engaging in fun and meaningful activities is sustainable.
- Aerobic exercise, stretching, and strength training are associated not only with cardiac and cognitive fitness but also improvement in mood (Schuch et al. 2016; Sharma et al., 2006). We recommend starting with easy, realistic goals, that take into account the patient's overall conditioning, the environment where the person lives, and readiness to change habits. A first step for sedentary patients is to increase movement in daily life, such as walking out of doors for 10–15 min a day preferably with a friend, human, or canine; using the stairs, if feasible; or using in-home exercise equipment or doing chair exercises in front of a window with a nature view for its innately calming effects (Jo et al., 2019).
- To begin improvement in nutrition, encourage eating more whole foods, less sugary and ultra-processed foods, more whole grain cereal, bread, and pasta, and reducing or eliminating red meat. Suggest incorporating fruits and vegetables at every meal (even at breakfast), such as mushrooms and spinach in an omelet of egg whites, sprinkling berries, nuts/seeds in cereal, salads, side dishes, and even desserts plus having extra vegetables as a main course. Give e-resources to the patient about healthy recipes that fit the culture and region.
- Lifestyle changes are challenging; we recommend offering group sessions, conducted virtually or in-person to reinforce and support dementia prevention strategies.

Closing Remarks

This chapter focused on the growing evidence that dementia can be delayed through modification in lifestyle, but there are limits to what following the recommendations can do. Just as the body of the most fit athlete eventually wears down with age, so does the brain. Unfortunately, dementia is often viewed as a defeat. Alzheimer's disease is feared in American society for many reasons including the stigmatizing stereotypes of loss of personhood, being shunned by others, the misconception that new learning of any kind is impossible, and the notion that the person living with dementia lacks total usefulness to his/her family and society.

A contrasting perspective is to view living with memory loss as a life stage characterized by staying in the moment, appreciating small joys, and having unexpected opportunities for increased closeness with family members. Just as in palliative care, the goal of treatment for the person with memory loss is to enhance quality and meaning to life.

The use of Montessori methods of learning and techniques such as spaced retrieval with people living with memory loss has shown that learning is possible and procedural memory skills such as piano playing, singing, reading and dancing remain intact in moderate to late stages of dementia (Camp et al., 2011; www.youtube.com/watch?v=wlAXKJfesBM). We challenge the notion that loss of personhood is inevitable with dementia. When caring for people living with dementia, a full emotional life can exist even if language is lost. Individuals with dementia may hold emotional memories of past relationships without the ability to identify them (Duffy, 1999).

Most, if not all of the strategies to promote brain health, can also be used by those living with dementia as well as with their caregivers to maximize their physical and emotional wellbeing. The goals of medical treatment are usually in the province of medication or surgery to cure or reduce symptoms. When dementia is diagnosed with no medications or surgical procedures for cure, "care" is what is left, as though the patient is actively dying rather than living on average eight to 20 more years. PCPs and BCPs can do a service to families and their patients with memory loss by emphasizing that behavioral interventions that improve quality of life are modalities of treatment, as potent as any drug, if not more so.

18.9.1 Examples of Biblio-Prevention

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Buettner, D. (2015). *The Blue Zones Solution: Eating and living like the world's healthiest people.* Washington DC: The National Geographic Society.

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18.9.2 Examples of Biblio-Therapy for Caregivers

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Mace, N. & Rabins, P. *The 36-Hour day, sixth edition: A Family Guide to caring for people who have Alzheimer Disease, other dementias, and Memory Loss*. Baltimore: Johns Hopkins Press Health Book.

Silverstone, B. & Hyman, H.K. (2008). *You & your aging parent*. New York: Oxford University Press.

Zeisel, J. (2009). *I'm still here: A breakthrough approach to understanding someone living with Alzheimer's.* New York: Penguin Group.

18.9.3 E-Health Prevention Tools

Mobile Apps

Alzheimer's Association-Alzheimer's Disease Pocketcard web version and Clinician Pocketcard app. A quick reference guide for clinicians.

Brain Performance Challenge, free mobile app developed by the Brain Performance Institute, University of Texas. Provides cognitive challenging exercises & tracking of progress.

Ted talk: Genova, L (TED talk, April 28, 2017). *What you can do to prevent Alzheimer's?*

Websites

http://alzheimersprevention.org provides info on "Four pillars" of dementia prevention including information on Kirtan Kriya meditation for cognitive health.
https://www.alz.org/help-support/brain_health/10_ways_to_love_your_brain developed by Alzheimer's Association.
http://brainwellness.com provides recipes and information on brain healthy nutrition by Nancy B. Emerson Lombardo, Ph.D.
http://www.cdc.gov/aging/publications/features/dementia-not-normal-aging.html info on the difference between normal, healthy aging and dementia.
https://www.cen4ard.com caregiver activities & training for health professionals by applied gerontologist, Cameron J. Camp, Ph.D.
https://www.centerforhealthyaging.com mental health and aging tips & resources for health professionals and older adults by geropsychologist, Paula Hartman-Stein, Ph.D.
http://www.dietaryguidelines.gov. Dietary Guidelines for Americans_2020–2025.
https://www.drreginakoepp.com/podcast on mental health and aging info by geropsychologist, Regina Koepp, PhD.
https://www.geron.org/programs-services/brain-health-cognitive-impairment-and-dementia developed by Gerontological Society of America (Fall 2020)
https://healthybrains.org/pillars info on foundations of brain health from the Cleveland Clinic.
www.Livingto100.Club weekly radio interviews, blogs and information on aging, including dementia prevention with geropsychologist, Joe Casciani, Ph.D.
www.ornish.com strategies on nutrition, stress management, physical fitness, and ways to feel emotionally supported by cardiologist and lifestyle medicine physician, Dean Ornish, M.D.
https://www.rebeccakatz.com recipes, blogs, videos on healthy nutrition from author of *The Longevity Kitchen.*
https://teepasnow.com caregiver information and programs by Alzheimer educator and occupational therapist, Teepa Snow.
https://www.youtube.com/channel/UCVgK5-w1dilMx7bPVB5yNug weekly dementia tips, strategies, and support by geropsychologist, Natali Edmonds, PhD.

Conflicts of Interest The authors declare they have no conflicts of interest.

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