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Lifestyle and health-related risk factors and risk of cognitive aging among older veterans☆

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Abstract Lifestyle and health-related factors are critical components of the risk for cognitive aging among veterans. Because dementia has a prolonged prodromal phase, understanding effects across the life course could help focus the timing and duration of prevention targets. This perspective may be especially relevant for veterans and health behaviors. Military service may promote development and maintenance of healthy lifestyle behaviors, but the period directly after active duty has ended could be an important transition stage and opportunity to address some important risk factors. Targeting multiple pathways in one intervention may maximize efficiency and benefits for veterans. A recent review of modifiable risk factors for Alzheimer's disease estimated that a 25% reduction of a combination of seven modifiable risk factors including diabetes, hypertension, obesity, depression, physical inactivity, smoking, and education/cognitive inactivity could prevent up to 3 million cases worldwide and 492,000 cases in the United States. Lifestyle interventions to address cardiovascular health in veterans may serve as useful models with both physical and cognitive activity components, dietary intervention, and vascular risk factor management. Although the evidence is accumulating for lifestyle and health-related risk factors as well as military risk factors, more studies are needed to characterize these factors in veterans and to examine the potential interactions between them.
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1. Introduction

Lifestyle and health-related factors represent an important category of risk factors for cognitive aging among veterans. Evidence is emerging supporting an association between several health factors and behaviors with risk of cognitive impairment and dementia including cardiovascular risk factors, physical and cognitive activity, nutrition, sleep quality, and smoking and alcohol use. Although veterans may be at increased risk of cognitive aging because of a unique set of military-related exposures [1], some lifestyle and health-related risk factors may also be elevated in veterans such as smoking and sleep disturbances [2,3]. It is estimated that in the general population, lifestyle and health-related risk factors may contribute to almost half of dementia cases [4],

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suggesting that further investigation of this constellation of risk factors could be a critical component of understanding risk of cognitive aging in veterans and developing effective dementia prevention strategies. This review will present the supporting evidence for major lifestyle and health-related risk factors for cognitive impairment and dementia (other military-related exposures and mental health risk factors will be reviewed elsewhere in this issue) and discuss the prevalence of these risk factors in veteran populations. Many lifestyle and health-related risk factors may emerge as a consequence of military service including behaviors that are potentially modifiable during active duty service.

2. Cardiovascular risk factors

A number of critical cardiovascular and metabolic risk factors have demonstrated strong relationships with cognitive decline and dementia, including hyperlipidemia, hypertension, and diabetes [5,6]. In epidemiologic studies, midlife vascular risk factors have been consistently associated with a risk of late-life dementia [5,7]. Estimates of these chronic conditions among veterans vary, but in one study of veterans using VA health-care data, 16% had diabetes and 37% had hypertension [8], the prevalence of dyslipidemia was estimated to be between 25% and 36% (Table 1) [9,10]. A comparison of veterans with nonveterans from the National Health and Nutrition Examination Survey indicates that the prevalence of hypertension was not significantly different between the two groups [11].

In observational studies, high blood pressure in midlife has been associated with an increased risk for both vascular dementia and Alzheimer's disease (AD) [12,13]. Hypertension may affect cerebral blood flow and increase vascular brain injury [14–16]; there is also evidence from mice models and epidemiologic studies to suggest that hypertension interferes with β-amyloid clearance [17,18]. An increasing number of studies also indicate that hypotension in late life could increase dementia risk because of the effects on cerebral blood flow [19]. Data from blood pressure treatment trials, such as Action in Diabetes and Vascular Disease (ADVANCE), Hypertension in the Very Elderly cognitive function assessment (HYVET-COG) and the Study on Cognition and Prognosis in the Elderly (SCOPE), vary with some demonstrating a benefit for dementia prevention and others reporting no effects, which may be a result of differences in the class of drugs used for hypertension therapy [20]. To further understand the effects of blood pressure treatment, the ongoing National Institutes of Health (NIH)–funded Systolic Blood Pressure Intervention Trial will monitor the course of cognitive decline with intensive blood pressure control [21].

Data from observational cohort studies indicate that high cholesterol levels could increase the risk of dementia, and both neuropathologic and observational studies of patients on statin therapies correspond with these findings [22]. High cholesterol may increase dementia risk by increasing production of β-amyloid and increasing β-amyloid aggregation, but few studies have distinguished between the effects of specific lipids such high- or low-density lipoproteins [22,23]. Translation of these findings to prevention interventions has been challenging as most randomized controlled trials have not resulted in any benefits from statin therapy [23]; however, the lack of positive results could be related to issues of blood-brain barrier permeability and timing of therapy [23].

The consistent observation that diabetes is associated with an increased risk of dementia could be the result of several pathways including disruption of insulin signaling necessary for brain function, increased accumulation of advanced glycation end products, and interference with β-amyloid clearance [24]. Meta-analyses suggest that the

Table 1
Prevalence of lifestyle and health-related risk factors among veterans

Risk factor	Prevalence in veterans (%)	Data sources
Cardiovascular risk factors		
Hypertension	36.8	1991–2001 VA Health Care System [8]
Dyslipidemia	29.5	1998–2001 VA Health Care System [10]*
Diabetes	15.6	1991–2001 VA Health Care System [8]
Obesity	37.4	2000 VA Health Care System [158]
Metabolic syndrome	25.0	2004–2005 VANCHCS [40]
Physical activity		
Meets recommended guidelines†	45.1	2003 BRFSS [50]‡
Sleep quality		
Insufficient sleep	22.7	2009 BRFSS [3]‡
Sleep apnea	2.9	1998–2001 VA Health Care System [159]
Alcohol use		
Alcohol misuse§	25.0	2005 EPRP Medical Record Reviews [160]
Smoking		
Current smoking	19.7	2011 VA Survey of Enrollees [161]
Nicotine dependence	14.9	2008–2009 VA Health Care System [162]

Abbreviations: VA, Veteran Affairs; VANCHCS, Veteran Affairs Northern California Health Care System; BRFSS, Behavioral Risk Factor Surveillance System; EPRP, External Peer Review Program of VA Medical Records.

*Data from six VA acute care medical centers.

†Meeting physical activity recommendations indicates ≥30 minutes of moderate activity on ≥5 d/wk or 20 minutes or more of vigorous activity on ≥3 d/wk.

‡Veterans who reported using VA Health Care.

§Alcohol misuse indicates positive screen on Alcohol Use Disorders Identification Test (AUDIT) or AUDIT-Consumption.

risk of both AD and dementia is higher in those with diabetes compared with those without diabetes [24,25]. Among older adults, diabetes is associated with a range of magnetic resonance imaging (MRI) outcomes including increased brain atrophy [26], increased ischemic lesions [27], and lower fractional anisotropy in white matter and greater diffusivity in regions such as the hippocampus [28]. Investigations of markers of glucose control suggest that there may be a U-shaped association with cognitive impairment in which both hyperglycemia and hypoglycemia are associated with an increased risk of dementia [29]. Preliminary treatment trials with intranasal insulin have been encouraging with studies reporting positive effects for cognition in patients with cognitive impairment [30].

The association between obesity and increased risk of dementia might be related to its role as a marker of vascular and inflammatory damage. In addition, adipose tissues secrete inflammatory proteins such as leptin, which could affect neurodegeneration [31]. Behavioral Risk Factor Surveillance System (BRFSS) data indicate that similar to the general population, rates of obesity in veterans are a concern [32,33]. Almost one-quarter of veterans meet the criteria for obesity, whereas more than half are overweight [33,34]. Although few studies have focused solely on weight loss for dementia prevention, a meta-analysis of weight loss trials reported benefits for attention and executive function primarily in obese subgroups; however, long-term randomized controlled trials are needed to determine the effectiveness of such interventions [35].

The metabolic syndrome, composed of several of the risk factors described previously, is another cardiovascular risk factor with strong evidence of an association with cognitive impairment and dementia [6,36,37]. Metabolic syndrome is defined as having at least three of the following five risk factors: abdominal obesity, high triglycerides, low high-density lipoprotein cholesterol level, high blood pressure, and high fasting blood glucose [38]. In 2006, it was estimated that among veterans without diabetes, 2 million may have the metabolic syndrome [39], and evaluation of data from the Veterans Affairs Northern California Health Care System found that 25% of veterans met the criteria for metabolic syndrome [40]. Several studies have identified an interaction between the metabolic syndrome, inflammation, and increased risk of cognitive impairment [6,41,42], and in a small study of community-dwelling older adults, metabolic syndrome was associated with microstructural changes in the brain, including magnetization transfer ratio peak height and diffusivity [43].

In general, the prevalence of cardiovascular risk factors in veterans is not elevated compared with nonveteran populations, but there may be subgroups of veterans that have higher prevalences of these risk factors, in particular those with a mental health diagnosis. Among Iraq and Afghanistan veterans enrolled in VA Health Care, those with a mental health diagnosis including posttraumatic stress disorder (PTSD), depression, adjustment disorders, anxiety, and substance and alcohol use disorders were more likely to have hypertension, hyperlipidemia, and obesity [44]. PTSD, in particular, may also be associated with greater likelihood of obesity and overweight as well as the metabolic syndrome [45,46]. Chronic stress could alter several pathways such as the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system leading to increased risk of cardiovascular disease [47]. In addition, other exposures associated with military service such as combat experience and Agent Orange exposure have been associated with elevated levels of cardiovascular risk factors [48,49].

3. Physical activity

Although active duty military members report high participation in physical activity, studies indicate that veterans do not maintain comparable levels of activity after military service [50,51]. Only 45% to 50% of veterans meet guidelines for sufficient physical activity, roughly similar to the percentages meeting recommended guidelines in nonveteran populations [50,52]. Furthermore, although most veterans recognize the importance of physical activity, they also report additional barriers to regular physical activity participation related to their military service including depression, injuries, and chronic pain [53,54]. Enforced body composition and fitness standards during military service [55] do not translate into postmilitary habits, and retirees have a prevalence of obesity at least comparable with their civilian peers [56]. The upper limit of permissible body fat in active duty service members older than 40 years is 26% and 36% for men and women, respectively, and some of the military services have more stringent limits [57]. These upper limits coincide with median values for body fat in the US nonmilitary population surveyed in the National Health and Examination Survey [58] indicating that half of older Americans would be too fat for active duty. The similarity of obesity rates between retired military and civilian population is particularly striking and supports the perception that there may be an increased risk for major weight gain within the first year of retirement from active duty. Such an effect of large overshoot body fat gain after exercise cessation has been observed in rodent models [59,60]. This concept of "retirement obesity" in veterans is a topic of current research interest specifically called out in a request for proposals from the National Institute of Diabetes and Digestive and Kidney Diseases.

As a protective health factor, physical activity may decrease the risk of cognitive aging by increasing oxygen saturation and neurogenesis and decreasing vascular risk factors, inflammation, and depressive symptoms [61,62]. In one study of older adults, habitual physical activity

was associated with lower levels of $A\beta_{1-42}$-to-$A\beta_{1-40}$ ratio and amyloid deposition in the brain, but conflicting results were reported by another study of older adults (cognitively normal or with mild cognitive impairment) [63,64]. A meta-analysis of prospective studies in nondemented older adults found that not only were high levels of physical activity protective against cognitive decline, but low-to-moderate activity levels were also protective [65]. Similar results were reported for a meta-analysis examining physical activity and risk of dementia [66]. In concordance with these findings, imaging studies also suggest that physical activity is associated with beneficial effects on brain structure [67] including increased gray matter volume [68] and better measures of white matter integrity (lower diffusivity and higher fractional anisotropy) [69,70], whereas low physical activity has been associated with increased brain atrophy [71].

Evidence from randomized controlled trials indicates that both aerobic exercise and resistance training could delay cognitive decline [72]. The findings from randomized controlled trials are still just emerging, but physical activity interventions in older adults have reported benefits for executive function, processing speed, delayed memory, and attention; positive effects have been shown for patients with mild cognitive impairment in particular [72].

4. Neuroprotective nutrition

In 2011, the Committee on Military Nutrition Research (CMNR) completed an important analysis of nutritional factors influencing susceptibility, protection, and recovery from military traumatic brain injury. This was intended to be only the first phase of a larger strategic assessment of neuroprotective nutrition, but, with the advent of new defense budget cuts, this became the last funded effort of this standing committee at the Institute of Medicine that has advised the Department of Defense on military nutrition research for 25 years. The comprehensive 431-page report provided an expert assessment of the state of knowledge and made recommendations for further investigation in neuroprotection [73]. Many of the same nutrients and supplements recommended for further research by the CMNR have emerged as potential disease modifiers in associational studies of AD and dementia, including n-3 fatty acids, flavonoids, antioxidants, and choline.

Some of these AD associations have also been supported by plausible mechanisms and have been explored in animal studies, but none of these nutrients and dietary components has been properly evaluated in randomized prospective studies. Part of the reason for this is that randomized controlled trials are expensive and failure of an expensive trial reduces willingness to embark on new trials, but there are other complications with nutrition studies. One of the advantages of nutritional modifiers of disease is that these tend to be affordable changes in normal behaviors rather than involving pharmaceutical treatments that invariably carry undesirable side effects, but the disadvantages are in being able to conduct studies of potentially large health impacts that may only be accrued through long-term habits (e.g., antioxidant intakes) and may interact with other behaviors such as activity patterns. Action on these important recommendations from the CMNR and for nutrients with potential benefit to disease modification for AD and dementia will depend on federal funding (e.g., NIH, US Department of Agriculture, and VA) as there is generally little commercial incentive in promoting health applications for foods relative to the investment incentive in pharmaceuticals.

Table 2
Summary of neuroprotective nutrients

Nutrient	Possible mechanism
Oleocanthal	Prevent aggregation of tau protein and reduce β-amyloid
Omega-3 fatty acids	Moderate chronic microglial inflammatory responses
	Protect against oxidative damage
Epigallicatechin	Hippocampal neurogenesis
	Anti-inflammatory
	Reduce β-amyloid and tau aggregation
Caffeine	Antagonize the A_{2A} adenosine receptor
	Potentiate BDNF action in the hippocampus
	Protect against oxidative damage
Choline	Acetylcholine precursor
Vitamins C and E	Protect against oxidative damage
	Reduce β-amyloid toxicity
Folate	Moderate plasma homocysteine

Abbreviation: BDNF, brain-derived neurotrophic factor.

Key components of the Mediterranean diet have biologically plausible mechanisms for suspected neuroprotective benefits that have been demonstrated in some epidemiologic studies (Table 2) [74]. The potent anti-inflammatory properties of oleocanthal, a component of extra virgin olive oil that was identified through its similar throat irritant properties, may offer a partial explanation for the benefits of the Mediterranean diet in AD and have been shown to prevent aggregation of tau protein and reduced β-amyloid accumulation in mice [75,76]. Similarly, omega-3 fatty acids found in high concentration in many fish are precursors for resolvins and protectins that may be important moderators of chronic microglial inflammatory responses to brain insults [77]. This may help to explain the lower prevalence of AD in countries with the highest fish consumption [78]. Epigallicatechin (EGC) has been much investigated as one of the important polyphenols in dark chocolate and green tea, two foods associated with health benefits and specific effects on hippocampal neurogenesis [79]. The effects of flavonoids such as EGC appear to be anti-inflammatory but may also involve neuronal signaling, with effects on brain-derived neurotrophic factor (BDNF) and other factors affecting memory, learning, and cognition [80]. In transgenic AD mice, EGC reduced β-amyloid and tau aggregation [81]. Caffeine in coffee and other foods has

specific neuroprotective effects that appear to be mediated through antagonism of the A_{2A} adenosine receptor and with actions that range from potentiation of BDNF action in the hippocampus to neuroprotective antioxidant activity [82,83]. Drinking three to five cups of coffee per day was associated with a decreased risk of dementia and AD in a Finnish cohort [84]. Transgenic AD mouse studies demonstrate caffeine protective and restorative benefits for memory and reduced β-amyloid accumulation [85]. Animal studies of oleocanthal, EGC, caffeine, and omega-3 fatty acids suggest antiamyloidogenic properties of these nutrients and possibly synergistic effects of some combinations [86]. Choline has long been pursued in research for neurophysiological effects in the cholinergic system; when combined with an omega-3 fatty acid and uridine in a drink form, the combination improved memory after administration to patients with early AD for 6 months [87]. Fruits and vegetables in the Mediterranean diet, such as berries and grapes, also provide antioxidant vitamins and nutrients. Reactive oxygen species are involved in neuronal damage and brain aging. Long-term antioxidant nutrition, in the form of supplements with Vitamins C and E in combination, has been associated with substantially reduced risk for AD compared with no supplement use, suggesting the possibility that antioxidants in the diet could delay AD onset [88]. Folate has also been considered for its role in moderating plasma homocysteine, which has strong associations as a risk factor for dementia and AD, and folate-deficient diets may increase AD risk [89,90].

The single identified neuroprotective dietary component in the US military diet is caffeine, which is ingested in high amounts estimated at a mean consumption rate of 285 mg/d, primarily in the form of coffee; 82% of soldiers consumed caffeine at least weekly. In the US military, caffeine is even provided in a chewing gum formulation in the First Strike Ration [91]. Service members are not prominent consumers of the nutrients and other dietary components that tend to be neuroprotective. For example, they tend to have diets low in omega-3 fatty acids as fish is not a popular meal, and except for one special meal with salmon (Kosher for Passover), there is no fish entrée in any operational rations. Vitamin use, including multivitamins that would usually include antioxidant levels of Vitamins C and E, does have a relatively high prevalence in service members, with half of all soldiers using a dietary supplement, including more than one-third of soldiers using a multivitamin [92]. This suggests opportunities for future neuroprotective nutrition designs of military operational rations with potentially high impact in modifying acute and long-term brain health and performance.

5. Cognitive and social activity

The likely protective effects of cognitive activity have given rise to the concept of cognitive reserve in which factors such as education could buffer the effects of neuropathologic damage associated with dementia. In a study of World War II veterans, participants reporting more intellectually demanding jobs had better cognitive performance in late life [93], and in a cohort of male twins from the National Academy of Sciences-National Research Council Twin Registry of World War II veterans and participants in the Duke Twins Study of Memory in Aging, midlife cognitive activity was associated with lower risk of dementia [94]. Cognitive engagement in activities such as games, puzzles, or reading has also been associated with lower risk of cognitive decline and dementia in elderly populations [95]. Furthermore, in a study of older adults, the effect of plasma β-amyloid on cognitive decline was attenuated by cognitive reserve (defined as a higher level of education or literacy) [96], and neuropathologic studies indicate that cognitive activity may increase neuronal density and cortical thickness (compensation), modifying the effects of cerebrovascular disease and increasing brain mass [97]. Similarly, one study found that the effects of educational attainment were more strongly associated with cognitive ability in late life than neurodegenerative pathology (measured by white matter intensities and hippocampal atrophy) [98]. Cohort studies also indicate that frequent cognitive activity could compensate for the effects of lower education [99], whereas lifetime cognitive activity was associated with lower amyloid deposition (early and midlife) in a small cross-sectional study [100].

Randomized controlled trials in both healthy and impaired individuals indicate that cognitive training may be beneficial and suggest that interventions targeting multiple domains may be better than those focused on a single domain, but the effects on dementia risk are still not confirmed [101]. Cognitive training in older adults over 12 weeks demonstrated benefits for cerebral blood flow, network connectivity, and white matter integrity [102].

Like cognitive activity, higher levels of social engagement and social networks have also been associated with lower cognitive decline and reduced risk of dementia in observational studies [103]. The benefits of social engagement may be linked to the mechanisms of cognitive reserve. Social activities could increase cognitive stimulation as well as enhance social support and influence. However, reverse causality may also be an underlying factor for this observed association. As dementia progresses, patients may be less able to engage in social activity [104]. Nevertheless, several long-term prospective studies with follow-up times of over a decade have also demonstrated similar protective relationships between social engagement and risk of dementia in both mid- and late life [105]. One MRI study suggests that high social engagement is associated with greater total brain and gray matter volumes [106]. There is some evidence from trials to suggest that increased engagement in social activity could be effective in lowering risk of cognitive decline and dementia [107,108].

Previous studies in veteran populations support a protective role for cognitive reserve and decreased risk of other psychiatric disorders including PTSD, major depression, and major anxiety disorder [109,110]. Similarly, higher levels of social support are associated with reduced risk of psychiatric comorbidities [111], but more studies are needed to understand the potential impact of cognitive and social activities on veterans' risk of dementia.

6. Sleep quality

Sleep disturbances are a major concern for veterans. In a recent study of active duty military personnel attending treatment facilities, one-quarter were diagnosed with mild obstructive sleep apnea and another quarter had moderate-to-severe apnea, whereas almost one-fourth of the sample also met criteria for insomnia, and 40% reported short sleep duration (<5 hours of sleep per night) [112]. Data from the BRFSS indicate that veterans are more likely to report sleep disturbances (not enough sleep and short sleep) compared with nonveterans [3], and in an observational study, older veterans also reported more sleepiness than controls [113].

Sleep quality is a critical emerging risk factor for cognitive aging [114]. Measures of sleep quality such as excessive daytime sleepiness, sleep duration, and sleep latency have been associated with dementia and cognitive impairment [115–117]. Disturbed sleep could affect synaptic plasticity and consolidation of memory [118–120]. Data from rodent models suggest that β-amyloid clearance may also occur during sleep, possibly mediated through aqueporin 4 [121,122]. A survey of veterans indicates that insufficient sleep and fatigue are common, but many veterans may not be receiving treatment for these symptoms [123].

Evidence is also accumulating for sleep-disordered breathing as a risk factor for cognitive impairment and dementia. Cross-sectional studies suggest that cognitive performance is worse in those with sleep-disordered breathing [124–126], and in a prospective study of older adults, sleep-disordered breathing was associated with an increased risk of dementia [127]. Sleep-disordered breathing has also been associated with decreased white matter integrity and lower gray matter volume [128,129].

Circardian rhythms are another characteristic of sleep that may be associated with cognitive impairment. Disruptions in circadian rhythms may be common during military service [130], and there is some evidence to suggest circadian variation in heart rate variability as it relates to autonomic dysfunction in Gulf War Illness [131,132], but little is known about circadian disturbances in sleep among veterans. In older adults, altered circadian rhythms, including decreased amplitude and robustness as well as shifted time of peak activity, have also been associated with higher risk of developing dementia [133]. Like cardiovascular risk factors, sleep disturbances, sleep-disordered breathing, and circadian rhythm alterations are associated with psychiatric comorbidities including PTSD [134–137].

7. Alcohol and smoking

Both alcohol and smoking are important lifestyle risk factors that could significantly affect dementia risk, and veterans may be more likely to engage in some of these behaviors [51]. Neuroimaging studies indicate that smoking may lead to both macro- and microvascular cerebral damage [14,138]. A meta-analysis of prospective studies indicates that compared with nonsmokers, current smokers had higher rates of cognitive decline and increased risk of dementia; however, former smokers did not have an increased risk of dementia compared with nonsmokers [139].

In contrast to smoking, studies have reported that there may be a J-shaped curve in risk associated with alcohol consumption such that moderate alcohol consumption is more protective than no consumption, but heavy alcohol consumption is associated with an increased risk of dementia [140]. A meta-analysis of epidemiologic studies found that moderate alcohol use was associated with decreased risk of AD and any dementia [141]. Proposed pathways of beneficial effects may be related to lowering lipid levels, modifying hormone levels, or, in the case of wine, antioxidant effects [142], but chronic alcohol abuse could be neurotoxic and increase risk of dementia [143].

Data from the BRFSS indicate that overall, veterans may not have riskier alcohol consumption patterns compared with nonveterans [144] but that specific groups such as older veterans and veterans who are college students may engage in riskier consumption patterns including heavy and binge drinking [144,145]. Similar population-based surveys also suggest that rates of smoking tend to be higher among veterans compared with nonveterans [2,51]. Results from the BRFSS indicate that the age-adjusted prevalence of current smoking was 27.0% among veterans, but the prevalence was even higher among younger veterans, between 36% and 40%, whereas the prevalence of smoking among younger nonveterans was between 22% and 30% [2]. Veterans with mental health diagnoses are also more likely to smoke [146].

8. Conclusion

In the United States, almost 60% of veterans are older than 60 years [147], and by 2030, projections suggest that there will be >7 million veterans older than 65 years [148]. As a result, cognitive impairment and dementia could have a significant impact on veterans' health-care costs and caregiver burden. Although military-related risk factors are an integral component in determining the risk of cognitive aging among veterans, lifestyle and health factors are also critical. Veitch et al. [149] estimated that by the year 2020,

about 63,000 cases of AD among veterans would be attributable to obesity, 75,000 to hypertension, 49,000 to dyslipidemia, 51,000 to low physical activity, 19,000 to diabetes, and 55,000 to smoking.

Because dementia has a prolonged prodromal phase, understanding effects across the life course could help focus the timing and duration of prevention targets. This perspective may be especially relevant for veterans and health behaviors. Studies suggest that the prevalence of certain health behaviors fluctuate over the life course, and although military service may impact the development and maintenance of healthy lifestyle behaviors [52,150], the period directly after active duty has ended could be an important transition stage to begin to address some of these risk factors [151,152].

Targeting multiple pathways in one intervention may maximize efficiency and benefits for veterans. A recent review of modifiable risk factors for AD estimated that a 25% reduction of a combination of seven modifiable risk factors including diabetes, hypertension, obesity, depression, physical inactivity, smoking, and education/cognitive inactivity could prevent up to 3 million cases worldwide and 492,000 cases in the United States [4]. Lifestyle interventions to address cardiovascular health in veterans may serve as useful models including the Self-Management to Prevent Stroke Program [153], POWER, an intervention of peer leaders to control hypertension [154], and MOVE!, a weight loss program [155]. A small number of randomized controlled trials have started to test the efficacy of multidomain interventions in general populations. These include the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability with physical and cognitive activity components, dietary intervention, and vascular risk factor management and the Multidomain Alzheimer Preventive Trial, which will test omega-3 supplementation and a multidomain intervention with cognitive training, physical training, and nutritional education [156]. The Prevention of Dementia by Intensive Vascular Care study will target multiple vascular risk factors including hypertension and hyperlipidemia through primary care management and counseling [157].

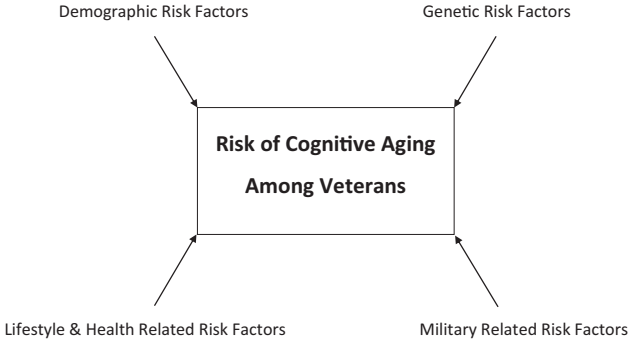

Fig. 1. Proposed risk factors for cognitive aging among veteran populations.

A number of issues must be investigated to fully understand the full spectrum of risk factors for cognitive aging in veterans (Fig. 1). The demographics of the veteran population continue to change with increasing racial/ethnic and gender diversity, and over time, aging cohorts of veterans may reflect different exposures and risk factors associated with service in different wars [148]. In addition, broad population trends toward sedentary lifestyles, and an increased risk of obesity could be an important factor for upcoming generations of veterans. As demonstrated by Barnes and Yaffe [4], the prevalence of these various risk factors in different populations could play an important role in evaluating risk and determining prevention targets. Although evidence is accumulating for lifestyle and health-related risk factors as well as military risk factors, more studies are needed to characterize these factors in veterans and to examine the potential interactions between them.

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