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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.