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Subjective Excessive Daytime Sleepiness and Frailty Progression in Veterans Over 50 With Insomnia

Mona Amirmazaheri
Walden University

Walden University

College of Health Sciences and Public Policy

This is to certify that the doctoral dissertation by

Mona Amirmazaheri

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the review committee have been made.

Review Committee
Dr. Howell Sasser, Committee Chairperson, Public Health Faculty
Dr. Peter Anderson, Committee Member, Public Health Faculty

Chief Academic Officer and Provost
Sue Subocz, Ph.D.

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Abstract

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Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health-Epidemiology

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Abstract

Frailty is common in aging veterans and linked to adverse outcomes. This retrospective cohort study of 6,824 veterans with insomnia examined whether excessive daytime sleepiness, sleep treatments, and PTSD affected frailty progression over four years. Frailty was measured using a validated index, with models adjusted for demographics and comorbidities, including chronic coronary insufficiency. Manuscript 1 showed that a higher Epworth Sleepiness Scale (ESS) score (range 0-24) was independently associated with a higher frailty index (FI) ($p < .001$). A clinical threshold of ≥11 indicated EDS and greater odds of frailty worsening compared to scores <11 (adjusted odds ratio (aOR) = 1.16, 95% CI [1.02, 1.32], $p = .021$). There was no significant interaction between ESS and time, suggesting that sEDS reflects persistently elevated frailty levels rather than accelerated decline. Manuscript 2 showed that nonpharmacologic sleep interventions were protective, while pharmacotherapy was associated with increased frailty risk. Cognitive behavioral therapy for insomnia was associated with lower odds of frailty worsening (aOR = 0.31, 95% CI [0.19, 0.53], $p < .001$), and continuous positive airway pressure therapy also reduced risk (aOR = 0.55, 95% CI [0.39, 0.76], $p < .001$). In contrast, sleep medications were associated with increased odds of frailty progression (aOR = 1.16, 95% CI [1.02, 1.32], $p = .021$). Manuscript 3 showed that PTSD was not associated with baseline frailty levels but showed a significant time interaction ($B = 0.001$, $p = .008$), indicating modest acceleration of frailty progression among affected veterans. Findings support positive social change through early sEDS screening and trauma-informed, nonpharmacologic sleep care to reduce frailty in veterans.

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Dedication

This dissertation is dedicated to those who stood beside me during one of the most difficult personal chapters of my life, a time of profound transition and emotional challenge beyond the academic journey.

To my beloved son, Dian, your presence gave me strength, purpose, and the courage to keep going. To my parents, whose unconditional love and support never wavered. To Armin, whose kindness & support helped me endure the darkest days. To Khatereh and Maryam, for your friendship, support, and faith in me when I needed it most.

Finally, I dedicate this work to the veterans whose experiences inspired this research. May this study serve, in some small way, to honor their resilience and improve the care they receive.

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To all Walden's faculty and staff who supported my academic progress, thank you for creating a learning environment that fostered both intellectual and personal growth.

To my family & friends, thank you for your enduring support throughout this process. Though your names appear in my dedication, your impact reaches into every chapter of this work.

Finally, to the veterans whose experiences form the heart of this research, thank you for your service and sacrifice. May this dissertation contribute to improving the care and understanding you so deeply deserve.

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Part 1: Overview

Introduction

Subjective excessive daytime sleepiness (sEDS) among elderly veterans aged 50 and older is a significant public health concern, particularly among those with insomnia. The effect of sEDS extends beyond individual health, influencing broader societal concerns such as safety, productivity, and economic stability. Veterans who experience unique stressors and health challenges have a higher prevalence of sleep disorders, which can exacerbate existing frailty and contribute to adverse health outcomes (Feng et al., 2024). EDS is characterized by an impaired ability to stay awake and alert during major waking episodes, resulting in periods of irrepressible need for sleep or unintended lapses into drowsiness or sleep (Pérez-Carbonell et al., 2022). EDS has been associated with increased frailty and morbidity, including cognitive impairment, reduced productivity, and a higher risk of accidents (Feng et al., 2024; Steier et al., 2023).

Frailty is an age-associated, multidimensional clinical syndrome that results from cumulative declines in physiological, functional, and cognitive systems, leading to increased susceptibility to stressors and adverse health outcomes (Tang et al., 2021; Zhang et al., 2023). The condition is characterized by a phenotype including unintentional weight loss, exhaustion, low physical activity, slowness, and weakness (Kim et al., 2022). It significantly elevates the risks of falls, hospitalization, disability, cognitive impairment, and mortality, making it a critical public health concern among older adults (Çavuşoğlu et al., 2021). Frailty is associated with a reduction in physiological reserve, limiting the body's ability to buffer stressors, and is often

quantified using the frailty index (FI), a validated metric ranging from 0 (no frailty) to 1 (complete frailty; Minici, 2023). Although frailty risk increases with age, modifiable factors such as physical inactivity, sleep disorders, and medical comorbidities contribute to its progression (Fan et al., 2022). Research indicates that frailty is not necessarily irreversible; targeted interventions addressing its underlying contributors have been shown to improve health outcomes and reduce the economic burden on healthcare systems (Zhang et al., 2023). Sleep characteristics, particularly sleep duration, have been identified as risk factors for frailty (Zhang et al., 2023). In this retrospective cohort study, I employ statistical analysis to examine the longitudinal association between sEDS and frailty progression among veterans aged 50 and older with insomnia. SEDS is measured using the ESS, and data on mediating factors, including mental health conditions and medical interventions, are extracted from electronic medical records (EMRs). Findings from this analysis provide empirical evidence to support the development of targeted interventions. SEDS is a significant public health concern due to its association with decreased cognitive function, increased accident risks, and impaired daily performance. About 20% of adults in the United States report daytime sleepiness sufficient to interfere with daily activities. EDS is also the most reported symptom among patients seeking evaluation at sleep clinics (Wu et al., 2024). EDS has the highest prevalence among adolescents, older adults, and shift workers. However, accurately estimating its prevalence remains challenging due to the subjective nature of the symptoms, variations in terminology, and inconsistencies in diagnosis and assessment methods (Steier et al., 2023). For aging veterans, who are already at increased risk of chronic health conditions,

the interaction between sEDS and frailty has been associated with reduced quality of life and increased healthcare utilization (Chuang et al., 2022). While prior studies have identified an association between EDS and various health risks, including the progression of frailty in aging populations, research specifically focused on veterans remains limited (Chuang et al., 2022). Veterans experience unique health challenges due to their service-related exposures, trauma, and psychological factors, which may exacerbate the effects of sleep disorders in ways not seen in other populations (Chuang et al., 2022). The relationship between sEDS and frailty in veterans, particularly those with insomnia, has not been extensively studied (Chuang et al., 2022).

Furthermore, longitudinal data on the effects of sEDS on frailty progression over time in this high-risk group are lacking, yet such data are essential for developing targeted, veteran-specific interventions (Chuang et al., 2022; Taylor et al., 2020). Frailty is a clinical condition associated with population aging and is common among older adults. Variability in measurement tools has led to differences in reported prevalence rates (Fan et al., 2022). Addressing this issue is crucial for improving individual health outcomes and reducing the broader healthcare and economic burdens (Fan et al., 2022). The prevalence of EDS increases exponentially with age and is associated with impaired balance, reduced gait speed, low physical activity levels, disability in daily activities, depression, and an increased risk of falls (Steier et al., 2023). Also, EDS has been associated with higher rates of incident disability and dementia, with its frequency increasing in parallel with the severity of cognitive decline (Fan et al., 2022). In this study, I examined the limited research on the longitudinal impact of sEDS on frailty

progression in veterans aged 50 and older with insomnia. Also, in this study, I assessed the longitudinal relationship between sEDS and frailty, including the role of potential mediators, to quantify the extent to which sEDS contributes to frailty progression among aging veterans. The assessment evaluates these mechanisms, particularly the mediating effects of mental health conditions and medical treatments.

Posttraumatic stress disorder (PTSD) is associated with higher rates of psychiatric and medical comorbidities, disability, substance abuse, and suicide, as well as increased healthcare utilization (Pattinson et al., 2020). Insomnia symptoms are associated with negative health outcomes, including falls, low health-related quality of life, and higher healthcare costs among older adults (Fan et al., 2022). Frailty and insomnia share some common risk factors and predict similar adverse outcomes (Fan et al., 2022). The findings of this research have significant implications for public health, clinical practice, and social change. By providing evidence-based insights into the effects of sEDS on frailty, the results may contribute to advancements in clinical interventions and health policies specifically tailored to aging veterans. These findings may also inspire further research and efforts to develop improved diagnostic and treatment strategies for managing sEDS and its impact on frailty, ultimately leading to better health outcomes, reduced healthcare costs, and an enhanced quality of life for veterans. Additionally, raising awareness of sleep health could foster broader public health initiatives and policies to prevent and manage sleep disorders in older adults. EDS is associated with a wide range of comorbidities, including sleep disorders, obesity, and psychiatric disorders

(Steier et al., 2023). Existing literature has also identified an increased risk of disability and mortality among individuals with EDS (Steier et al., 2023).

Background

Insomnia and sEDS are prevalent among the aging population and have particularly severe implications for veterans aged 50 and older. This demographic often experiences unique health challenges due to a combination of age-related changes and the physical and psychological demands of military service (Colvonen et al., 2020). Insomnia, characterized by difficulty falling or staying asleep or waking up too early, leads to insufficient sleep quality and duration, which can severely impair daytime functioning (Zimmerman et al., 2024). SEDS, on the other hand, refers to a persistent feeling of sleepiness during daytime hours despite adequate sleep at night, often resulting from untreated or poorly managed sleep disorders (Zimmerman et al., 2024). The International Classification of Sleep Disorders defines EDS as the inability to stay awake and alert during major waking periods, resulting in unintended lapses into drowsiness or sleep (Pérez-Carbonell et al., 2022). Sleep disturbances are frequently reported among veterans. A study of veterans in primary care setting found that 41% of patients had symptoms of insomnia, and 47% met high-risk criteria for sleep-disordered breathing based on Berlin Questionnaire results (Ranney et al., 2022). Veterans have a high prevalence of risk factors such as chronic alcohol consumption and obesity, which increase susceptibility to insomnia and sleep-disordered breathing (Ranney et al., 2022). A review of Veterans Health Administration (VHA) outpatient clinic records indicated that up to 16% of veterans have sleep apnea, although only 2.9% had received a formal

clinical diagnosis. (Ranney et al., 2022). Recent military conflicts, including those in Iraq and Afghanistan, have exposed U.S. military personnel to combat, hazardous security duties, and stressful noncombatant roles that disrupted their sleep-wake cycles during extended deployments (Pattinson et al., 2020). Evidence suggests that combat exposure may negatively affect sleep patterns among returning veterans (Pattinson et al., 2020). A recent survey of 2,525 soldiers returning from Iraq found that approximately 30% reported persistent sleep disturbances 3 to 4 months after their return to the United States following their tour of duty (Pattinson et al., 2020).

Moreover, the rates of sleep disturbance were higher among soldiers who had sustained a head injury, with as many as 58.3% reporting sleep problems following a head injury that involved a loss of consciousness (Pattinson et al., 2020). Long-term data indicate that sleep disturbances may persist or worsen over time, as some studies of Vietnam War veterans have reported prevalence rates as high as 90%. (Pattinson et al., 2020). Although sleep disturbances are prevalent among returning combat veterans, the etiology and nature of these disturbances remain poorly understood. Most research on sleep disorders in this population has focused on veterans diagnosed with PTSD, a debilitating anxiety disorder characterized by symptoms of hyperarousal, avoidance, and re-experiencing (Simon et al., 2024). Recent estimates indicate that probable PTSD affects approximately 5% to 20% of returning combat veterans, with some studies reporting prevalence rates as high as 33% to 39% (Mooney, 2020; Pattinson et al., 2020). Sleep disruption, including nightmares and insomnia, is a core feature of PTSD (Pattinson et al., 2020). A variety of other sleep-related disorders have also been

identified in patients with PTSD, including EDS, obstructive sleep apnea (OSA), periodic leg movement disorder, sleep terrors, nocturnal anxiety attacks, and sleep avoidance (Nagy et al., 2022; Pattinson et al., 2020). Some studies suggest that the severity of sleep disturbance correlates with the severity of PTSD symptoms (Nagy et al., 2022; Pattinson et al., 2020). The disruption of sleep among patients with PTSD is often attributed to autonomic hyperarousal and limbic activation, which are proposed to underline the psychophysiological basis of the disorder (Swift, 2020). For individuals with PTSD, heightened arousal can interfere with sleep onset and contribute to reduced sleep quality. Some studies propose that the increased arousal and sleep disruption in patients with PTSD may eventually lead to the development of sleep disorders such as EDS (Pattinson et al., 2020). The association between sleep disorders and adverse health outcomes is well-documented (Pattinson et al., 2020). Studies have shown that sleep disorders are prevalent among older adults and are associated with significant morbidity and mortality (Keil et al., 2020). For instance, research indicates that insomnia and sEDS contribute to cognitive decline, higher risk of accidents, impaired daily functioning, and reduced quality of life (Keil et al., 2023; Hou et al., 2020).

Frailty is a geriatric syndrome characterized by diminished physiological reserve, reducing the body's capacity to respond to stressors and increasing vulnerability to adverse health outcomes (Tang et al., 2021). This condition is associated with an increased risk of falls, cognitive impairment, hospitalization, and mortality, significantly impacting the health and well-being of older adults (Alqahtani, 2021; Çavuşoğlu et al., 2021; Kim et al., 2022; Henrique et al., 2023; Pourmotabbed et al., 2020; Tang et al.,

2021; Wai & Yu, 2020; Wen et al., 2023; Xu et al., 2024; Zhang et al., 2023). However, the specific long-term effects of sEDS on frailty progression in older veterans remain insufficiently studied. EDS has also been linked to increased rates of incident disability and dementia, with its frequency rising in parallel with the severity of cognitive decline (Steier et al., 2023). Sleep disorder symptoms are associated with adverse health outcomes, including falls, low health-related quality of life, and institutionalization, which overlap with frailty-related consequences and contribute to higher healthcare costs among older adults (Fan et al., 2022). Although frailty is not necessarily irreversible, targeted interventions addressing its risk factors may serve as effective strategies for prevention and recovery (Zhang et al., 2023). Sleep is a fundamental biological process essential for various restorative functions, including emotion regulation and memory consolidation, muscle and tissue repair, and stress hormone regulation (Steier et al., 2023).

Previous Research and Existing Literature

Numerous studies have examined the impact of insomnia and sEDS on various health outcomes (Liguori et al., 2024). EDS has been associated with multiple contributing factors, such as sleep disorders, medical and neurologic conditions, and psychiatric disorders. Its prevalence ranges from 10% to 33% in adult populations and may increase with age (Steier et al., 2023). Cohort studies have indicated an association between EDS and adverse health outcomes, though results remain inconclusive (Steier et al., 2023). EDS has been associated with poor medical health, cognitive impairment, reduced productivity, poor work performance, higher risks of automobile accidents, and

medical errors (Liguori, 2024; Steier et al., 2023). In nursing homes, EDS affects a substantial proportion of older adults and has been associated with low physical activity, falls, reduced functionality, cardiovascular risk factors, malnutrition, dysphasia, depression, cognitive impairment, and poor self-rated health (Steier et al., 2023). Among veterans, sleep disturbances are often compounded by service-related factors such as trauma and stress, which may contribute to conditions like PTSD (Colvonen et al., 2020). PTSD may further exacerbate sleep problems, creating a cycle that negatively impacts overall health and well-being (Mooney, 2020; Swift, 2020). This interplay between these factors necessitates a comprehensive examination of how sEDS influences frailty progression in this population (Emrich, 2024).

Insomnia and sEDS symptoms are common among military veterans (Ranney et al., 2022). In addition, a recent study of older veterans with impairment in activities of daily living showed that 71% experienced at least mild daytime sleepiness, and among veterans in a primary care setting, 41% reported insomnia symptoms (Ranney et al., 2022). EDS has also been associated with an increased risk of falls and injury, adversely affecting postural control, attention, and cognition, which are critical for maintaining balance and optimal walking performance (Wen et al., 2023; Zhang et al., 2023). The association between EDS, frailty, and fall risk is significantly relevant, as more than one-third of adults aged 65 and older experience falls each year (Steier et al., 2023). Interventions for managing insomnia and EDS include prescribed sleep medications, CBT-I, and CPAP therapy. Prescribed sleep medications Rxs refer to pharmacological treatments, which are commonly used but vary widely in effectiveness and potential side

effects. This study includes data on whether patients use prescribed sleep medication, allowing for assessment of their overall impact on frailty progression without analyzing specific medication types. CBT-I is an evidence-based, nonpharmacologic treatment designed to address the cognitive and behavioral factors that contribute to insomnia (Manber et al., 2023). By improving sleep hygiene and modifying behaviors that interfere with sleep, CBT-I has been associated with improved sleep quality and reduced insomnia symptoms (El Basiouny et al., 2023; Manber et al., 2023). In this study, CBT-I was examined to assess its effectiveness in mitigating EDS symptoms, which may, in turn, influence frailty progression by improving both physical and mental function through enhanced sleep quality (El Basiouny et al., 2023; Manber et al., 2023).

CPAP is a primary treatment for sleep apnea, which often co-occurs with insomnia. CPAP therapy delivers air pressure through a mask to keep airways open during sleep, reducing episodes of interrupted breathing and improving sleep quality (Aboussouan et al., 2023). Because untreated sleep apnea can worsen EDS and contribute to insomnia, CPAP therapy is included in this study to assess its role in managing EDS and its potential impact on frailty risks (Aboussouan et al., 2023). CPAP therapy may improve frailty outcomes by reducing daytime fatigue, enhancing cognitive function, and supporting physical balance—factors impacted by both EDS and frailty (Aboussouan et al., 2023). These interventions provide critical insights into the management of sEDS and frailty in aging veterans, as they target specific mechanisms that may influence the frailty progression. Evaluating their impact within this cohort may help identify effective strategies for reducing the frailty burden, improving quality of life, and minimizing

healthcare costs associated with EDS in older adults, through direct and indirect mechanisms that increase physical and cognitive vulnerability, including reduced physical activity and impaired balance, which contribute to muscle weakness and gait instability, key indicators of frailty.

Among the aging population, frailty is a strong predictor of poor health outcomes, leading to increased healthcare utilization, diminished quality of life, and higher mortality rates. The chronic nature of EDS has been associated with fatigue and exhaustion, key frailty criteria that increase the risk of adverse outcomes such as falls and functional decline. Additionally, EDS has been associated with cognitive decline and reduced executive function, compounding frailty-related risks, including falls, hospitalization, and mortality. It frequently cooccurs with physical and mental morbidities such as diabetes, cardiovascular disease, and depression, further exacerbating its impact (Zhang et al., 2023; Steier et al., 2023). The interaction between EDS and frailty progression is especially relevant among veterans, who frequently experience additional health stressors due to service-related factors and may have a higher risk of frailty progression than their nonveteran counterparts. Studies have identified associations between EDS and worsening frailty outcomes as EDS may contribute to an increase in physical, psychological, and cognitive vulnerability, potentially accelerating frailty in at-risk populations, such as veterans (Steier et al., 2023; Fan et al., 2022). EDS is linked to physical inactivity, disability in daily activities, depression, and a higher mortality rate (Steier et al., 2023). Its prevalence will increase with age, affecting nearly one in three individuals over 80 (Steier et al., 2023). Long sleep duration and EDS have been

associated with higher rates of incident disability and increased mortality in older adults (Steier et al., 2023). Both short and long sleep durations have been associated with frailty (Zhang et al., 2023). Despite evidence indicating that unrecognized or poorly managed sleep disorders can result in adverse health outcomes, many patients remain undiagnosed or untreated. Estimates suggest that 80% to 90% of individuals with clinically significant sleep disorders may remain undiagnosed (Byrne et al., 2021). In a representative sample of U.S. adults, 26% of survey respondents met the criteria for high-risk obstructive sleep apnea (Byrne et al., 2021), compared to an estimated prevalence of approximately 4% to 10% (Byrne et al., 2021).

An upward trend in office visits for sleep disorders was observed among U.S. adults from 1999 to 2010 (Byrne et al., 2021). However, it remains unclear whether this increase reflects a true rise in sleep disorder prevalence, greater awareness among physicians and patients, or a combination of both (Byrne et al., 2021). Variability in case definitions, diagnostic criteria, population demographics, and the presence of comorbid conditions may also contribute to inconsistencies in population-based estimates of sleep disorder prevalence (Byrne et al., 2021). CPAP is the first-line treatment for moderate to severe obstructive sleep apnea-hypopnea syndrome (OSAHS) and has been shown to mitigate fully or partially many of its adverse effects when used consistently (Sánchez-De-La-Torre et al., 2023). Despite its efficacy, empirical studies indicate that adherence to regular CPAP use (≥4 h daily) ranges from 30% to 60% (Sánchez-De-La-Torre et al., 2023). Research conducted in predominantly White OSAHS populations has identified demographic, polysomnographic, social, and psychological factors affecting CPAP

adherence. For example, age, BMI, daytime sleepiness, OSAHS severity, CPAP pressure, optimal CPAP titration, outcome expectancies associated with CPAP use, and perceived confidence in CPAP use (self-efficacy) have all been associated with adherence (Sánchez-De-La-Torre et al., 2023). In a sleep intervention involving military personnel and veterans with OSA and insomnia, improvements in sleep quality were associated with significant reductions in depression and PTSD symptoms (Pattinson et al., 2020; Milinovic et al., 2024).

Gaps in Knowledge

Despite the established associations between sleep disorders and various health outcomes, several gaps remain in the current literature. First, limited longitudinal research has examined the specific impact of sEDS on frailty progression in veterans aged 50 and older. Most studies have focused on general populations or have not distinguished between different types of sleep disorders (Kim et al., 2022; Çavuşoğlu et al., 2021; Wai & Yu, 2020; Tang et al., 2021; Henrique et al., 2023; Pourmotabbed et al., 2020; Zhang et al., 2023; Wen et al., 2023; Alqahtani, 2021; Xu et al., 2024). Second, the potential mediating roles of mental health conditions, such as PTSD, and medical interventions, including CBT-I and prescribed sleep medications, have not been thoroughly investigated in this context (Mirchandaney et al.; 2023). Examining the effect of CBT-I, CPAP therapy, and prescribed sleep medications is essential, as each intervention addresses key components of sleep disorder management that may reduce the fatigue, cognitive decline, and physical instability associated with sEDS. These effects could potentially mitigate frailty progression (Steier et al., 2023; Fan et al., 2022).

Conceptual Framework

This dissertation applies two primary theoretical frameworks to address these gaps: the stress process model (SPM) and the Clinical Epidemiology Framework. The SPM (Aneshensel et al., 2015), developed by Leonard I. Pearlin and colleagues in the 1980s, quantifies the pathways through which stressors, including sEDS, influence individuals' health outcomes by impacting psychological resilience, coping mechanisms, and physiological responses. This model outlines the interactions among stressors, coping mechanisms, and resources, providing a framework for evaluating their effects on mental and physical health outcomes. The Clinical Epidemiology Framework, introduced by Alvan R. Feinstein (2001), applies epidemiological methods to clinical practice. This framework is used to assess the patterns, causes, and effects of health conditions within defined populations, particularly in clinical settings. By integrating these frameworks, the analysis evaluates relationships between sEDS and frailty progression, examining both direct effects and the roles of mediating factors to generate empirical evidence on these interactions.

Rationale for the Study

These frameworks were selected based on their relevance to the research questions and the nature of the study. The Stress Process Model provides a structure for examining the mechanisms through which sEDS, as a significant stressor, impacts frailty, accounting for the roles of coping mechanisms and resources. The Clinical Epidemiology Framework provides a robust methodological foundation for assessing the impact of medical interventions on health outcomes in a clinical population. Together, these

frameworks support a comprehensive analysis of the interactions between sEDS, frailty, PTSD, and medical interventions.

Overview of the Manuscripts

This proposed retrospective cohort study examines EMRs from the VHA, covering patient encounters from 2019 to 2023. The initial cohort includes veterans aged 50 and older identified using sleep-related International Classification of Diseases (ICD) codes (ICD-9 or ICD-10) or records of sleep-related services based on specific Current Procedural Terminology (CPT) codes (Hong, Y., & Zeng, M. L., 2023; Elkin, P. L., & Brown, S. H. (2023). These codes include 0203T, 0204T, 95782, 95783, 95800, 95801, 95806, 95808, 95810, 95811, 95819, 95821, 95822, 95827, 95828, 99508, G0398, G0399, and G0400. The cohort is further refined to include individuals with documented ESS scores and a diagnosis of insomnia. A natural language processing (NLP) (Lane & Dyshel, 2025) algorithm is developed and validated to extract ESS scores from unstructured free-text physician notes. EDS is defined as an ESS score of ≥11. Patients are categorized into two groups: Normal-ESS (n-ESS) with ESS scores of 0-10 and high-ESS (h-ESS) with ESS scores of 11-24. (Gu et al., 2025). Data were obtained from the VHA's corporate data warehouse (CDW), a relational database aggregating patient information from all VHA facilities. The data include diagnoses, medication prescriptions, laboratory results, vital signs, and physician notes. Participants are identified based on sleep-related ICD codes and validated case-finding algorithms for insomnia and ESS. Relevant treatments, including medications and CBT-I, are documented. This study has received approval from the institutional review board (IRB)

of Baylor College of Medicine (BCM) and the Research and Development Committee of the Michael E. DeBakey VA Medical Center (MEDVAMC).

Manuscript 1: Impact of Subjective Excessive Daytime Sleepiness on Frailty Progression in Veterans

Research Question: What is the longitudinal impact of sEDS on frailty progression in veterans aged 50 and older with insomnia after controlling for age, sex, BMI, and the CCI?

Null Hypothesis (H_0): There is no significant longitudinal association between sEDs and frailty progression in veterans after adjusting for age, sex, BMI, and CCI.

The primary exposure variable in this study is the sEDS, measured using ESS scores. The outcome variable is frailty progression, measured by changes in the Frailty Index over time. The baseline FI is defined at the date of insomnia diagnosis, with and follow-up FI measurement conducted 4 years after the insomnia diagnosis. Covariates, including age, sex, BMI, and the CCI, are measured at the time of the baseline FI assessment to account for potential. Confounding. For measurement, sEDS levels are assessed based on ESS score, while frailty progression is quantified by changes in FI at two time points: at the index date of insomnia diagnosis and 4 years later. This study applies the SPM to examine the role of sEDS as a stressor influencing frailty. SPM conceptualizes stress as a multidimensional process involving exposure to stressors, individual appraisal of stressors, and the availability of coping mechanisms and resources. Within this framework, stress is modeled as an interaction between life events

or chronic conditions, an individual's perception of these stressors, and the coping strategies employed. The model posits that the effects of stress are modified by social and personal resources that may buffer or exacerbate health outcomes. Data were sourced from VHA Electronic Medical Records. Extracted variables include demographic data (age, BMI, race, ethnicity, sex), health status indicators including CCI score, sleep-related assessments such as ESS scores, insomnia diagnosis identified using ICD codes, and sleep-related services based on CPT codes, and outcome measures including longitudinal changes in FI.

Manuscript 2: Association Between Medical Interventions and Frailty Progression in Veterans With Insomnia and Abnormal ESS Scores

This manuscript examines the association between medical interventions, sleep medication, CBT-I, and CPAP, and frailty progression among veterans with insomnia and abnormal ESS scores.

Research Question: What is the association between medical interventions (sleep medication, CBT-I, and CPAP and the progression of frailty among veterans aged 50 and older with insomnia and abnormal ESS scores after controlling for age, sex, BMI, and CCI?

> Null Hypothesis (H_0): There is no statistically significant association between medical interventions (sleep medication, CBT-I, and CPAP) and frailty progression in veterans aged 50 and older with insomnia and abnormal ESS scores after adjusting for age, sex, BMI, and the CCI.

The primary exposure variables in this study are clinical treatments, including sleep medication, CBT-I, and CPAP. The outcome variable is frailty progression, measured through changes in the FI over time. Covariates include age, sex, BMI, and CCI to account for potential confounding effects. Clinical treatments are documented in EMRs, and health outcomes are assessed using FI measurements at baseline and follow-up time points. In this study, the Clinical Epidemiology Framework has been applied to evaluate the relationship between medical interventions and frailty progression. The framework is a quantitative approach used in epidemiology to study the patterns, causes, and effects of health and disease conditions in defined populations, focusing on patient populations and clinical settings. It provides a structured approach to assessing disease processes, diagnostic methods, prognostic factors, and treatment outcomes within clinical populations. By incorporating epidemiological principles, this study quantifies the associations between treatment modalities and health outcomes, providing empirical evidence on the effectiveness of interventions in frailty progression. The objective is to generate evidence that informs clinical decision-making and patient care by identifying the prevalence, incidence, risk factors, and outcomes of diseases within clinical environments. Specifically, within the study, I examine frailty as the outcome, assessing its prevalence, incidence, risk factors, and progression in veterans receiving different sleep-related treatments. Data were sourced from EMRs, which provide comprehensive longitudinal patient information. Extracted variables include demographic data (age, BMI, race, ethnicity, sex), health status indicators CCI, sleep-related assessments ESS

scores, treatment information (sleep medication, CBT-I, CPAP, prescribed drugs), and outcome measures (FI changes over time).

Manuscript 3: Does Frailty Progression Differ Between Veterans with sEDS and Insomnia with or without PTSD?

This manuscript examines whether the presence of PTSD influences frailty progression in veterans aged 50 and older with insomnia and sEDS. The analysis utilizes data from the VHA's corporate data warehouse (CDW) to examine the interactions between sEDS, PTSD, and frailty progression.

Research Question: What is the relationship between being diagnosed with PTSD and the progression of frailty among veterans aged 50 and older with insomnia and sEDS, after controlling for age, BMI, race, ethnicity, sex, and the CCI?

Null Hypotheses (H_0): There is no relationship between being diagnosed with PTSD and the progression of frailty among veterans after controlling for age, BMI, race, ethnicity, sex, and CCI.

The primary exposure variable is sEDS, measured by ESS scores. PTSD status serves as a mediating variable and is determined based on documented PTSD diagnoses identified using ICD codes in the VHA EMRs. The outcome variable, frailty progression, frailty progression, is assessed by evaluating changes in the FI at two specific time points. The baseline FI is recorded at the time of the insomnia diagnosis, and the follow-up FI is measured 4 years after this baseline date. Control variables, including age, sex, BMI, and CCI, are also recorded at baseline to account for potential confounding effects. Measurements include sEDS levels, determined using ESS scores, and PTSD status, both

assessed at the baseline. Frailty progression is measured by comparing FI measurements at baseline and follow-up to evaluate changes over the 4 years. In this study, I applied the SPM to examine the interaction between sEDS and PTSD and their combined effect on frailty progression. SPM conceptualizes stress as a dynamic process influenced by exposure to stressors, individual appraisal of stressors, and the availability of coping resources. This framework models PTSD as a chronic stressor that may exacerbate frailty progression through physiological and behavioral pathways. The model further accounts for the modifying role of social and personal resources in buffering or amplifying the effects of stress on health outcomes. Data were sourced from VHA Electronic Medical Records, providing a comprehensive data set for longitudinal analysis. Extracted variables include demographic data (age, BMI, race, ethnicity, sex), health status indicators (CCI, health conditions including insomnia diagnosis and other comorbid conditions), sleep-related assessments (ESS scores, insomnia diagnosis using ICD codes, and sleep-related services using CPT codes), treatment information (sleep medication, CBT-I, & CPAP), outcome measures (FI changes over time), and mental health variables (documentation of PTSD).

Significance

Advancing Knowledge in Discipline

This dissertation outlines the complex relationships between sleep disorders, frailty, and comorbid conditions in older veterans. The research addresses a critical gap in literature by focusing on sEDS and its impact on frailty progression. While previous studies have established the general health consequences of sleep disorders, limited

research has investigated the longitudinal effects of sEDS, specifically on frailty among older veterans (Gabelle et al., 2017; Nakakubo et al., 2016; Sun et al., 2020). This study contributes to the field by providing detailed insights into the role of sEDS, in combination with insomnia and PTSD, in frailty progression over time.

Implications for Clinical Practice

The findings from this study may inform clinical practices related to the management of sleep disorders and frailty in older adults. The results highlight the potential value of comprehensive sleep assessments and targeted interventions for veterans who may have a high risk of conditions. By providing evidence-based recommendations, this research supports the integration of effective treatment strategies, including sleep medication, cognitive-behavioral therapy for insomnia CBT-I, and CPAP therapy into routine clinical care. Implementing these approaches may enhance management strategies, improve patient outcomes, and contribute to a better quality of life for veterans.

Policy Implications

The findings of this research may inform health policy decisions, particularly in the context of veteran healthcare. By identifying the potential impact of sEDS on frailty and the possible benefits of targeted interventions, the study underscores the need for policies that prioritize sleep health in the veteran population. Evidence from this analysis may support resource allocation strategies aimed at improving access to comprehensive sleep disorder management, which could help mitigate frailty-related complications among veterans.

Contributions to Positive Social Change

Enhancing Veteran Well-being

Improving the health and well-being of older veterans is one of the main objectives of this study. Investigating the specific impact of sEDS on frailty may provide findings that inform strategies to enhance quality of life for this vulnerable population. Addressing sleep health in veterans has the potential to improve physical and mental health outcomes, thereby reducing the burden of disease and disability among veterans.

Reducing Healthcare Costs

Effective management of sleep disorders and frailty has the potential to reduce healthcare costs by preventing frailty progression and reducing the incidence of associated health complications. Identifying interventions that mitigate frailty risk may contribute to decreased healthcare utilization and expenditures. This is particularly relevant within veteran healthcare systems, where resource constraints and high service demand necessitate cost-effective strategies for improving patient outcomes.

Raising Awareness

Disseminating research findings may increase awareness of the critical role of sleep health in the veteran population and the public. Increased awareness has the potential to facilitate earlier diagnosis and intervention for sleep disorders, which may contribute to improved health outcomes and reduced societal burden of conditions such as sEDS and frailty.

Informing Future Research

Finally, this dissertation establishes a foundation for future research in sleep medicine, geriatric psychiatry, and veteran health by examining the associations between sEDS, insomnia, PTSD, and frailty. The findings contribute to identifying potential research directions, including the evaluation of additional interventions, the identification of new mediating factors, and the investigation of underlying mechanisms driving these associations. The significance of this dissertation extends beyond the immediate findings by generating evidence that may inform clinical practice, influence policy, and contribute to public health initiatives aimed at improving veteran health outcomes. The comprehensive approach taken in this study provides a framework for improving sleep health and frailty management in this vulnerable population, which may lead to improved quality of life and reduced healthcare burden.

Summary

This dissertation outlines a critical and underexplored aspect of veteran healthcare by examining the impact of sEDS on frailty progression in veterans aged 50 and older with insomnia. Through a comprehensive, multimanuscript approach, the study indicates potential gaps in the existing literature, provides evidence to inform clinical practice, and provides data-driven insights for health policy decisions. The first part of this dissertation establishes an overview of the relevance of sEDS and its impact on frailty progression, particularly in older veterans with insomnia. The introduction provides context for the broader implications of sleep disorders in this population, highlighting their public health significance.

Additionally, sEDS and its association with frailty progression are identified as key research areas requiring further investigation to improve health outcomes for veterans. The background section includes a systematic review of the literature, outlining established associations between sleep disorders and adverse health outcomes. However, a critical gap remains in longitudinal research, specifically examining the effects of sEDS on frailty among veterans. The conceptual framework integrates the SPM and the Clinical Epidemiology Framework to provide a structured approach for quantifying the pathways through which sEDS influences frailty progression. The overview of the manuscripts section outlines the specific research aims and methodologies of the three interconnected studies. In the first Manuscript, the direct association between sEDS and frailty progression using the SPM to quantify the influence of coping mechanisms has been examined. In the second manuscript, the effectiveness of medical interventions, such as sleep medication, CBT-I, and CPAP therapy, in mitigating frailty progression, by applying the Clinical Epidemiology Framework, has been evaluated. In the third manuscript, the combined effects of sEDS and PTSD on frailty progression, applying the SPM to analyze the complex interaction between these conditions, has been examined. The significance section outlines the study's implications for sleep medicine, geriatric psychiatry, and veteran healthcare by providing empirical findings on the association between sEDS and frailty. The findings support the development of evidence-based clinical recommendations for managing sleep disorders in older veterans and offer data-driven insights for policy decisions that prioritize sleep health in veteran care. Raising awareness of the impact of sleep disorders and establishing a foundation for future

research on additional interventions and mediating factors are further objectives of this analysis. The first part of the dissertation has established the framework for a comprehensive investigation of the research problem through the three interconnected manuscripts. Each manuscript systematically explores specific research questions, methodologies, and analytical strategies to assess the relationships between sEDS, frailty, PTSD, and medical interventions. By integrating findings across these manuscripts, the analysis provides a multidimensional perspective on the problem, contributing to the broader goal of improving health outcomes for aging veterans. In Part 2, each manuscript has been presented in detail, outlining research questions, methodological approaches, and statistical analyses used to evaluate the effects of sEDS on frailty progression. The integration of these findings provides evidence to inform clinical practices, health policies, and future research initiatives focused on mitigating frailty in this high-risk population.

Part 2: Manuscripts

Impact of Subjective Excessive Daytime Sleepiness on Frailty Progression in Veterans Aged 50+ With Insomnia

Mona Amirmazaheri

Department of Public Health, Walden University

Supported by the Department of Veterans Affairs, Michael E. De Bakey VA Medical Center (MEDVAMC), Baylor College of Medicine (BCM)

All findings and conclusions are solely those of the authors.

Outlet for Manuscript

Sleep Medicine is an ideal venue for "Impact of Subjective Excessive Daytime Sleepiness (sEDS) on Frailty Progression in Veterans." The manuscript addresses a prevalent, clinically consequential sleep symptom—daytime sleepiness—in an aging, high-risk population and links it to a validated geriatric outcome (Frailty Index) using a large, real-world VHA cohort. The study's longitudinal design, use of the ESS as both categorical and continuous exposure, and application of linear mixed models and adjusted logistic regression align with the journal's emphasis on rigorous clinical/epidemiologic methods and translational relevance. Findings that higher ESS is independently associated with a persistently higher frailty level (no ESS×time effect) and greater odds of frailty worsening provide actionable evidence to inform screening and risk stratification in sleep clinics caring for older adults. The work integrates perspectives from sleep medicine, gerontology, and veteran health, directly serving the journal's mission to bridge research and practice on diagnosis, outcomes, and management of sleep disorders.

Key words: Subjective Excessive Daytime Sleepiness (sEDS); Epworth Sleepiness Scale (ESS); Frailty Index; Insomnia; Veterans; Longitudinal Cohort

Highlights:

- Large VHA cohort (N=6,824; ≥50 years with insomnia): FI measured at baseline and ~4-year follow-up with adjusted LMM and logistic models.
- sEDS–frailty association: Each 1-point higher ESS corresponded to ~0.001 higher FI (p<.001); ESS≥11 increased odds of frailty worsening (aOR=1.16; 95% CI 1.02–1.32).

- Trajectory pattern: No ESS×time interaction—sEDS marks a higher frailty level, not a faster rate of increase.
- Covariates: Higher BMI and CCI and male sex are associated with higher FI; older age is inversely related to worsening (survivorship dynamics).
- Clinical implication: Routine ESS screening can support frailty risk stratification and targeted management in older veterans.

Abstract

Subjective excessive daytime sleepiness (sEDS) is common in older adults and may signal elevated frailty risk; veterans ≥50 with insomnia is especially vulnerable. This research was conducted to test whether sEDS is associated with frailty level and change over 4 years. A retrospective cohort study was conducted using Veterans Health Administration (VHA) corporate data warehouse electronic medical records (2019–2023), including veterans with documented Epworth sleepiness scale (ESS) and insomnia (n=6,824). Frailty was quantified by the frailty index (FI) at baseline and 4-year follow-up. Analyses used linear mixed modeling (LMM) for FI trajectories and logistic regression for frailty worsening (FI_worsen=1), adjusting for age, sex, BMI, and CCI. ESS was modeled continuously and categorically (≥11 vs <11); time was coded 0 and 4 years. Higher ESS was associated with higher FI across time (LMM main effect); each 1-point ESS increase corresponded to ~0.001 higher FI (p<.001). Compared with ESS<11, ESS≥11 predicted greater odds of frailty worsening (aOR=1.16, 95% CI 1.02–1.32; p=.021). The ESS×time interaction was not significant, indicating that sEDS did not accelerate FI change. Male sex, higher BMI, and higher CCI were associated with greater frailty and worsening; older age showed an inverse association with worsening, consistent with survivorship. Results were consistent when ESS was modeled continuously and categorically and were robust to alternative coding of FI (continuous vs binary). Under the stress process model, sEDS appears to act as a chronic stressor that sustains a higher frailty burden rather than steepening decline. Findings support ESS screening in older veterans with insomnia and sleep-focused interventions (CBT-I,

CPAP, physical activity/weight management, medication review) as components of frailty risk stratification in VHA care.

Introduction

Problem Focus

Subjective excessive daytime sleepiness (sEDS), defined as the inability to stay awake and alert during major waking episodes, is a significant public health concern due to its association with cognitive impairment, increased accident risk, and reduced productivity. Veterans, a population exposed to unique stressors and health challenges, have a higher prevalence of sleep disorders, which may contribute to frailty progression and adverse health outcomes. In this study, I examine the longitudinal association between sEDS and frailty progression in veterans, with a specific focus on those diagnosed with insomnia.

Significance/Importance

Frailty, an age-related syndrome characterized by a decline in physiological reserve, is associated with increased vulnerability to stressors and adverse health outcomes, such as falls, hospitalization, and mortality. Veterans aged 50 and older, particularly those with insomnia and sEDS, are considered a high-risk population due to unique service-related stressors and comorbidities. Findings from this study may contribute to clinical practices and health policies aimed at improving sleep health and mitigating frailty progression in this vulnerable group. By focusing on the interplay between sEDS and frailty, this analysis examines a critical gap in the literature, providing

empirical data to support targeted interventions that enhance quality of life and reduce healthcare burdens for aging veterans.

Theoretical Framework

The stress process model (SPM), developed by Leonard I. Pearlin and colleagues, serves as the theoretical foundation for this research. The SPM provides a framework for quantifying the interaction between stressors, such as sEDS, coping resources, and mechanisms, and their association with mental and physical health outcomes. In this study, sEDS is conceptualized as a chronic stressor measured by ESS scores, with frailty progression assessed by changes in the FI over time. Key control variables include age, sex, BMI, and the CCI. This framework provides a structured approach for quantitatively assessing the association between sEDS, persistent physiological and psychological strain, and frailty in older veterans. Applying SPM facilitates a structured quantitative evaluation of the mechanisms underlying the relationship between sEDS and frailty, integrating evidence from sleep medicine, gerontology, and veteran health.

Relevant Scholarship

Existing literature has extensively documented the adverse effects of sleep disorders on health outcomes, particularly in older adults (Alqahtani, 2021; Byrne et al., 2021; Çavuşoğlu, 2021; Henrique et al., 2023; Merlino et al., 2020; Soysal et al., 2021). SEDS has been linked to cognitive decline, increased risk of accidents, and diminished daily functioning (Wu et al., 2024; Zimmerman et al., 2024). Studies have shown that veterans experience a disproportionately high prevalence of sleep disorders, including insomnia, obstructive sleep apnea, and other sleep-related conditions (Sweetman, 2023;

Mysliwiec et al., 2020; Mooney, 2020). However, despite the well-established association between sleep disorders and various health outcomes, there is limited research that has examined the longitudinal impact of sEDS on frailty progression in veterans. Frailty is a multidimensional geriatric syndrome characterized by an increased risk of falls, hospitalization, and mortality (Sun et al., 2023). It is commonly assessed using the FI, which measures the accumulation of deficits across multiple domains (Sun et al., 2023). While previous studies have examined the impact of sleep disorders on general health, limited research has evaluated the specific association between sEDS and frailty (Kansagra, 2020; Hauri, 2021; Ravyts & Dzierzewski, 2024; Ribeiro et al., 2024). In this study, I examine this association in the veteran population, a group with an increased risk for both sleep disorders and frailty due to age and service-related health conditions.

SPM provides a structured framework for analyzing the potential association between sEDS and frailty progression in older veterans. Originally developed to examine the impact of chronic stressors on health outcomes, the SPM outlines the interaction between stressors (e.g., sEDS), coping resources, and long-term health trajectories (e.g., frailty progression; Zhang et al., 2024). Within this framework, sEDS is conceptualized as a persistent physiological and psychological stressor that, when prolonged, is associated with homeostatic resilience and accelerates biological aging. Chronic stress exposure has been linked to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, increased systemic inflammation, and impaired neurocognitive function, all of which are correlated with the accumulation of deficits characteristic of frailty (Zhang et al., 2024). SPM provides a structured approach for quantifying the extent to which

individual differences in coping resources—such as access to healthcare or behavioral adaptations—moderate the effects of sEDS on frailty risk. Veterans with greater physiological reserve and stronger coping mechanisms may experience a slower rate of frailty progression, while those with limited resources may have an increased rate of health decline due to the cumulative burden of sleep disruption and systemic stress responses (Zhang et al., 2024).

Furthermore, SPM provides a theoretical basis for quantifying the potential buffering effects of targeted interventions. Cognitive-behavioral therapies for insomnia (CBT-I), structured physical activity programs, and pharmacological interventions may be associated with reductions in the adverse impact of sEDS by modulating stress burden and enhancing physiological resilience (Whitty et al., 2020). Applying SPM in this study provides a basis for hypothesizing that sEDS acts as a chronic stressor associated with the depletion of physiological reserves over time, which may contribute to an increased rate of frailty progression among older veterans, particularly those with additional health vulnerabilities.

Research Questions and Design

The central research question of this study is: What is the longitudinal association between sEDS and frailty progression in veterans aged 50 and older with insomnia, after controlling for age, sex, BMI, and CCI?

To examine this question, the study utilizes a retrospective cohort design with data from the Veterans Health Administration (VHA) electronic medical records (EMRs). The primary independent variable is sEDS severity, measured by ESS scores, while the

dependent variable is frailty progression, measured by changes in the FI over time. Control variables include age, sex, BMI, and CCI, which are incorporated to adjust for potential confounders in the association between sEDS and frailty. The study applies SPM to examine the association between sEDS, as a stressor, and frailty progression. By analyzing high-risk population-older veterans with insomnia- this research aims to provide empirical evidence that may contribute to clinical decision-making and policy development in veteran healthcare.

Methods

Study Approval and Data Source

This study was conducted following approval from the Institutional Review Board at Walden University, Baylor College of Medicine (BCM), and the Research and Development Committee of the Michael E. DeBakey VA Medical Center (MEDVAMC). The primary data source was the VHA's CDW, a comprehensive relational database that integrates patient data from all VHA facilities nationwide. The CDW contains detailed records of inpatient and outpatient encounters, including diagnoses, medications, laboratory results, vital signs, and physician notes. The data collection period spanned from 2019 to 2023, focusing on sleep-related service encounters. The study cohort included veterans aged ≥50, a demographic with an increased prevalence of sleep disorders and frailty. Veterans with documented International Classification of Diseases (ICD-9 or ICD-10) codes for sleep disorders or associated CPT codes for sleep studies during this period were identified for inclusion. These codes captured a range of sleep-related services and conditions, ensuring a representative study population. The data set

established a longitudinal framework for analyzing the association between sleep disorders and frailty progression while accounting for medical, psychological, and demographic factors. Utilizing CDW's extensive repository of patient records, the study quantifies the relationship between sleep disorders and frailty among older veterans, allowing for a comprehensive assessment of these associations.

Cohort Selection

The study cohort consists of 6,824 veterans with documented ESS scores, identified through medical visits associated with specific CPT codes for sleep studies and polysomnography procedures. The sample size is determined to provide adequate statistical power for analyzing the association between sEDS and frailty progression. Eligibility criteria require participants to have both a recorded ESS score and a clinical diagnosis of insomnia. A validated natural language processing (NLP) algorithm has been used to extract ESS data from unstructured physician notes, ensuring precise identification of sEDS. The ESS, a standardized instrument for measuring daytime sleepiness severity, assigns scores ranging from 0 to 24, with higher values indicating greater sleepiness. EDS is operationally defined as an ESS score of ≥11. Participants are categorized into two groups: normal-ESS (n-ESS, ESS 0–10; n = 3,859) and high-ESS (h-ESS, ESS 11–24; n = 2,965). Control variables, including age, BMI, sex, race, ethnicity, and CCI, are identified using machine learning algorithms. Adjusted odds ratios aOR and 95% confidence intervals CI are calculated, using the n-ESS group as the reference category. This retrospective cohort design establishes a methodologically

rigorous framework for quantifying the longitudinal association between sEDS and frailty progression while adjusting for key demographic and health-related confounders.

Variables and Data Sources

Data were collected at two predefined time points: baseline (corresponding to the initial diagnosis of insomnia) and a 4-year follow-up period. This longitudinal design provided a framework for assessing frailty progression, with the FI serving as the primary outcome measure.

Dependent Variable: Frailty Progression

Frailty progression was measured using the FI at baseline and the 4-year follow-up. FI is a continuous measure that reflects the accumulation of health deficits across multiple domains, including physical, cognitive, and social factors. It is calculated as the proportion of health deficits present, with each deficit coded as present (1) or absent (0). FI scores range from 0 (no frailty) to 1 (complete frailty), with higher scores indicating greater frailty. For analytical purposes, FI scores were categorized as Robust ($FI \leq 0.10$), Pre-frail ($FI > 0.10$ and $FI \leq 0.20$), and Frail ($FI > 0.20$) (Minici, D., 2023). The study also incorporated the concept of frailty worth, defined as the difference between the frailty index at follow-up and baseline (FI_final & FI0). Frailty worth was categorized as:

0: No worsening of frailty (stable or improved health status).

1: Worsened frailty status (decline in health).

This classification provided a structured approach for assessing frailty progression, with an emphasis on participants who experienced worsening frailty during the study period (Kaskirbayeva et al., 2023).

Independent Variable: Subjective Excessive Daytime Sleepiness

SEDS was assessed using ESS, a validated self-reported instrument designed to measure daytime sleepiness. The ESS consists of eight items in which respondents rate their likelihood of dozing off in various everyday situations (e.g., watching TV, or sitting quietly after lunch). The total ESS score ranges from 0 to 24, with higher scores indicating greater daytime sleepiness severity. In this study, sEDS was defined as an ESS score of ≥11. Participants were categorized as Normal-ESS (n-ESS) (ESS 0–10), & High-ESS (h-ESS) (ESS 11–24).

Demographic and Health Data

Comprehensive demographic and health data were collected to adjust for potential confounders and facilitate subgroup analyses, Age: Grouped as <50 years, 50–65 years, and >65 years to assess age-related trends in frailty progression; Sex: Classified as male or female; Race: Categorized as White, Black, or Other; Ethnicity: Classified as Hispanic or Non-Hispanic; BMI: Categorized as non-obese (<30) and obese (≥30) (Mahajan, D., & Mohajan, H. K., 2023); CCI: Used to quantify comorbidity burden based on diagnoses in the year before baseline. CCI scores were categorized as Low comorbidity (CCI 0–1), & High comorbidity (CCI ≥2) (Kachlíková et al., 2020).

Data Sources

The study utilized EMRs from the VHA CDW, a comprehensive database that aggregates patient data from all VHA facilities nationwide. CDW contains detailed records on inpatient and outpatient encounters, diagnoses, medications, laboratory results, vital signs, and physician notes. Sleep-related diagnoses were identified using ICD-9/10

codes, while sleep-related procedures were identified using CPT codes. The study population consisted of veterans aged ≥50, a demographic with an increased prevalence of sleep disorders and frailty. This structured approach provides a detailed assessment of the association between sleep disorders, demographic and health variables, and frailty progression in the veteran population.

Statistical Analysis Strategies

To analyze the longitudinal association between sEDS and frailty progression, a linear mixed model (LMM) was implemented in SPSS. This model accounted for repeated measures of the FI over time, incorporating participant ID as a random effect and time as a fixed effect. The primary variable of interest was the fixed effect of sEDS (categorized by ESS scores), with age, sex, BMI, and CCI as control variables. Interaction terms between time and ESS were examined to assess differential effects on frailty progression.

Results

The analytic cohort comprised 6,824 veterans aged 50 years and older with insomnia and documented ESS scores, obtained from the VHA CDW, a comprehensive source of longitudinal electronic medical records for veteran populations. Veterans were selected based on documented insomnia and available sleepiness assessments, consistent with prior work noting high insomnia prevalence among veterans and its comorbid burden (Byrne et al., 2021; Mysliwiec et al., 2020; Sweetman, 2023). FI was assessed at baseline and a 4-year follow-up using the cumulative deficit approach described in the gerontological literature (Kaskirbayeva et al., 2023; Minici, 2023). Inclusion required

valid data on ESS, FI at both time points and core covariates. Missingness was minimal (e.g., 36 cases [0.5%] missing for age), and complete within-group data were available for the key continuous variables used in the ESS-stratified summaries. All available data were included in the descriptive analyses. Subsequent inferential analyses used linear mixed models with random intercepts for participants to model FI trajectories over time. Fixed effects included time (coded as 0 = baseline, 4 = follow-up), ESS (continuous and categorical), age, sex, BMI, and CCI; the interaction between time and ESS tested whether subjective daytime sleepiness modified frailty progression. A secondary mixed-effects logistic model examined frailty worsening (FI_worth) as a binary outcome.

Table 1 displays the key continuous characteristics stratified by ESS. Veterans with high sEDS (High-ESS; ESS ≥ 11) were slightly younger (M = 60.81 years, 95% CI [60.54, 61.09] than those with normal sleepiness (Normal-ESS; ESS < 11; M = 62.54 years, 95% CI [62.29, 62.80]). Mean BMI was modestly higher in the High-ESS group (M = 31.80, 95% CI [31.58, 32.02]) compared to Normal-ESS (M = 31.23, 95% CI [31.04, 31.41]). Baseline frailty (FI0) and follow-up frailty (FI_final) were greater among High-ESS veterans (FI0: M = .11, 95% CI [.10, .11]; FI_final: M = .12, 95% CI [.11, .12]) versus Normal-ESS (FI0: M = .09, 95% CI [.09, .09]; FI_final: M = .10, 95% CI [.09, .10]). CCI means were similar (High-ESS: M = 1.40, 95% CI [1.33, 1.46]; Normal-ESS: M = 1.43, 95% CI [1.37, 1.48]). Significant differences by ESS were observed for age group, PTSD status, sex, race, ethnicity, obesity status, baseline and follow-up frailty categories, FI_worth, intervention receipt (Rx_cat2), CBT-I exposure, and CPAP usage. CCI did not differ significantly by ESS.

There was no statistically significant difference in the distribution of ΔFI between the two sleepiness groups: Mann-Whitney U = 5,692,277.50, Z = −0.362, p = .718. Given the large sample size, this null bivariate finding suggests that the sEDS alone(unadjusted) was not associated with the ΔFI. (See Figure 1; Table 3.) The relationship between ESS and frailty progression, operationalized dichotomously as FI_worth (0 = no worsening, 1 = worsened), was evaluated with a chi-square test of independence. Veterans with High-ESS had a higher rate of frailty worsening (19.5%) than those with Normal-ESS (16.8%), and the difference was statistically significant, χ^2 (1, N = 6,824) = 8.14, p = .004. The effect size (Phi = .035) indicates a small but meaningful unadjusted association between elevated subjective sleepiness and frailty worsening. (See Figure 2; Table 4.)

Unadjusted findings: ΔFI did not differ by ESS group (Mann–Whitney U=5,692,277.50, Z=−0.362, p=.718; Figure 1; Table 3). The proportion with frailty worsening (FI_worth=1) was 19.5% in High-ESS and 16.8% in Normal-ESS (χ^2[1, N=6,824] =8.14, p=.004; Phi=.035; Figure 2; Table 4).

A binary logistic regression was conducted to evaluate whether high sEDS (High-ESS vs. Normal-ESS) was independently associated with frailty worsening (FI_worth = 1), adjusting for age, sex, race, and obesity. All predictors were entered simultaneously. The overall model was statistically significant, χ^2 (5) = 135.84, p < .001, indicating that the combination of variables reliably distinguished between veterans who did and did not experience frailty worsening. After adjustment, high ESS remained a statistically significant predictor of frailty worsening. Adjusted logistic regression (Table 5) showed that sEDS (ESS≥11) was associated with higher odds of frailty worsening (aOR 1.16,

95% CI 1.02–1.32). Male sex and obesity were associated with increased odds, whereas older age and race (vs reference) were associated with lower odds. Full coefficients and p-values are reported in Table 5.

A linear mixed model was estimated to examine the association between sEDS, sex, ESS, CCI, age, BMI, and time with FI, while accounting for within-person correlation through repeated measures. Patient ICN was specified as the subject with time treated as the repeated measure under an unstructured covariance structure. The model was fit using restricted maximum likelihood (REML) with Satterthwaite approximation for denominator degrees of freedom. Interaction terms—including ESS_cat × time, ESS_cat × BMI, ESS_cat × Age, ESS_cat × CCI, and ESS_cat × Sex—were included to assess whether the effect of ESS on FI varied across these dimensions. The Type III tests of fixed effects indicated that several predictors had statistically significant associations with FI. Specifically, In the linear mixed model (Table 6), ESS (continuous) was positively associated with FI after adjustment (≈0.001 FI units per ESS point; $p<.001$). FI increased over follow-up; higher BMI and higher CCI were associated with higher FI, with a small sex difference. No ESS interactions with time, BMI, age, CCI, or sex was significant. Estimates of fixed effects in the Linear mixed model clarify effect directions and magnitudes (Table 6). ESS (continuous) was positively associated with FI after adjustment ($\beta\approx0.001$ FI units per ESS point; $p<.001$), implying that a 5-point higher ESS corresponds to ~0.005 higher FI. FI increased over follow-up (time coded 0 and 4 years; $\beta\approx0.005$ for 4 years; $p<.001$). Higher BMI ($\beta\approx0.002$ per kg/m²; $p<.001$) and higher CCI ($\beta\approx0.009$ per point; $p<.001$) were also associated with higher FI, whereas age showed no

independent association. The sex effect was small. No interactions of ESS with time, BMI, age, CCI, or sex were significant (all $p>0.06$). Full estimates and 95% CIs are provided in Table 6.

Therefore, the model demonstrates that higher subjective ESS scores, greater comorbidity burden, higher BMI, male sex, and advancing time are independently associated with increased frailty index, while the categorical distinction of high versus normal ESS did not produce a significant adjusted difference in marginal means and did not interact meaningfully with time or other modifiers to alter those trajectories. Table 6 presents the full fixed effects estimates, and Figure 3 depicts adjusted frailty trajectories by ESS and sex. Figure 3 presents the estimated marginal means of the FI from the linear mixed model, stratified by sEDS (Normal-ESS vs. High-ESS) and sex (female = 0, male = 1), with all other covariates held at their sample means. Among veterans with Normal-ESS, male individuals had a higher adjusted FI (approximately .098) than female individuals (approximately .089), consistent with the main effect of sex in the model. In the High-ESS group, the sex difference narrowed markedly: both women and men had similar, lower adjusted FI values (approximately .072 for each), such that the elevated sleepiness appeared to attenuate the sex disparity seen in Normal-ESS. The confidence intervals around all four estimates overlap substantially, indicating that none of these stratified differences, whether between ESS within sex or between sexes within ESS, constitute statistically robust interaction effects. This visual pattern aligns with the inferential results showing nonsignificant ESS_cat × sex and ESS_cat × time interactions,

suggesting that the influence of high subjective sleepiness on frailty operates largely independently of sex and does not differentially change over the measured interval.

Table 1

Continuous Variable Descriptives By ESS

Variable	Normal-ESS (n = 3,859) M (95% CI)	High-ESS (n = 2,965) M (95% CI)
Age (years)	62.54 [62.29, 62.80]	60.81 [60.54, 61.09]
CCI	1.43 [1.37, 1.48]	1.40 [1.33, 1.46]
BMI	31.23 [31.04, 31.41]	31.80 [31.58, 32.02]
FI_0	.09 [.09, .09]	.11 [.10, .11]
FI_final	.10 [.09, .10]	.12 [.11, .12]

Note. Means are accompanied by 95% confidence intervals. Skewness and kurtosis indicated mild-to-moderate non-normality for CCI and FI measures (see diagnostics).

Table 2

Categorical Variable Distributions by ESS And Chi-Square Tests

Variable	χ^2 (df)	p	Effect Size	Notable Pattern
Age (50–65 vs >65)	57.21 (2)	<.001	—	ESS higher in 50–65
PTSD presence	8.19 (1)	.004	small (≈.035)	Higher in High-ESS
Sex	6.28 (1)	.012	small	High-ESS more in male individuals
Race (White, Black, Other)	78.13 (2)	<.001	.107	Black/Other prevalent in High-ESS
Ethnicity (Hispanic)	4.96 (1)	.026	small	Higher High-ESS among Hispanic
BMI (Obese vs not)	6.44 (1)	.011	small	High-ESS in Obese
FI_0	7.57 (2)	.023	small	Less robust in High-ESS
FI_final	17.39 (2)	<.001	small–moderate	Worse frailty in High-ESS
FI_worth (worsening)	8.14 (1)	.004	small	More worsening in High-ESS

Rx_cat2 (intervention)	5.79 (1)	.016	small	Slight difference by ESS
CBT-I receipt	13.78 (1)	<.001	small–moderate	Fewer High-ESS received CBT-I
CPAP usage	7.63 (1)	.006	small	Differed by ESS
CCI	1.86 (1)	.172	—	No significant difference

Note. Effect sizes reported where available; "—" denotes not applicable or not reported.

Table 3

Mann-Whitney U Test Comparing The ΔFI by ESS

ESS	n	Mean Rank	Sum of Ranks
Normal-ESS	3,859	3,405.07	13,140,147.50
High-ESS	2,965	3,422.18	10,146,752.50
Test Statistic		Value	
Mann-Whitney U		5,692,277.50	
Wilcoxon W		13,140,147.50	
Z		−0.362	
p (two-tailed)		.718	

Note. The variable labeled "F" in the source output must be clarified in the manuscript (e.g., change in FI over time [ΔFI] versus baseline FI) to make interpretation unambiguous.

Table 4

Cross-Tabulation of FI_Worth by ESS

FI_worth	Normal-ESS (0)	High-ESS (1)	Total
0 (no worsening)	3,210 (83.2%)	2,387 (80.5%)	5,597 (82.0%)
1 (worsened)	649 (16.8%)	578 (19.5%)	1,227 (18.0%)
Total	3,859	2,965	6,824

Note. $\chi^2 = 8.14$, $p = .004$; Phi = .035.

Table 5

Logistic Regression Predicting FI_Worth

Predictor	B	SE	Wald	df	p	aOR	95% CI

High-ESS (vs Normal)	0.149	0.064	5.36	1	.021	1.16	[1.02, 1.32]
Age (higher)	−0.645	0.075	74.00	1	<.001	0.53	[0.45, 0.61]
Male sex	0.541	0.123	19.26	1	<.001	1.72	[1.35, 2.19]
Race	−0.148	0.053	7.71	1	.005	0.86	[0.78, 0.96]
Obese (vs non-obese)	0.288	0.066	19.10	1	<.001	1.33	[1.17, 1.52]
Constant	−0.570	0.225	6.43	1	.011	0.57	—

Note. Interpretation is relative to reference categories: Normal-ESS, lower age, female sex, reference race group, and non-obese. aOR = adjusted odds ratio; CI = confidence interval.

Table 6

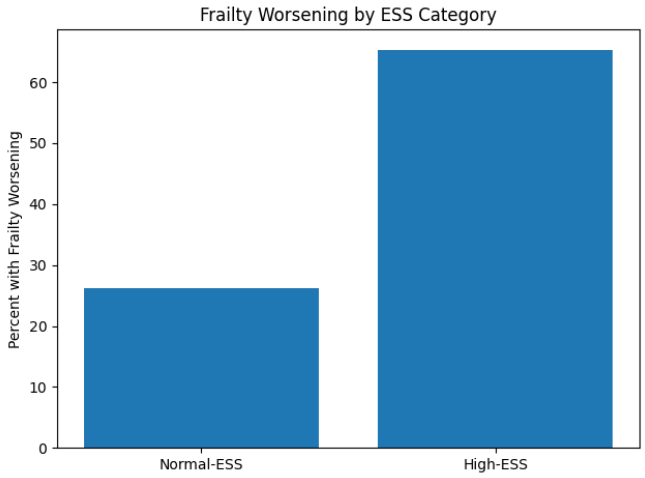
Linear Mixed Model Fixed Effects Predicting The Frailty Index

Predictor	Estimate	SE	df	t	p	95% CI (Lower-Upper)
(Intercept)	.019	.017	6821.76	1.08	.280	(−.015, .053)
ESS_cat (High vs Normal)	.052	.023	6822.66	2.29	.020	(.007, .096)
Sex (Male vs Female)	.011*	.005	6813.03	−2.09	.037	(−.021, −.001)
ESS	.001	<.001	6813.03	4.29	<.001	(.001, .002)
CCI	.009	.001	6813.03	10.93	<.001	(.008, .011)
Age	.000	<.001	6813.03	−.60	.546	(−.001, .000)
BMI	.002	<.001	6813.03	6.42	<.001	(.001, .002)
time	.005	<.001	6822.03	14.60	<.001	(.004, .005)
ESS_cat × time	.000	<.001	6822.03	−.78	.437	(−.001, .001)
ESS_cat × BMI	0b	—	6813.03	—	.209	(—)
ESS_cat × Age	−.001	<.001	6813.03	−1.85	.064	(−.001, 3.00E-05)
ESS_cat × CCI	.001	.001	6813.03	.69	.492	(−.001, .003)
ESS_cat × Sex	0b	—	6813.03	—	.975	(—)

Note. Parameters marked “0b” are constrained as redundant (reference combinations). Covariates are evaluated at their sample means for marginal means estimation.

Figure 1

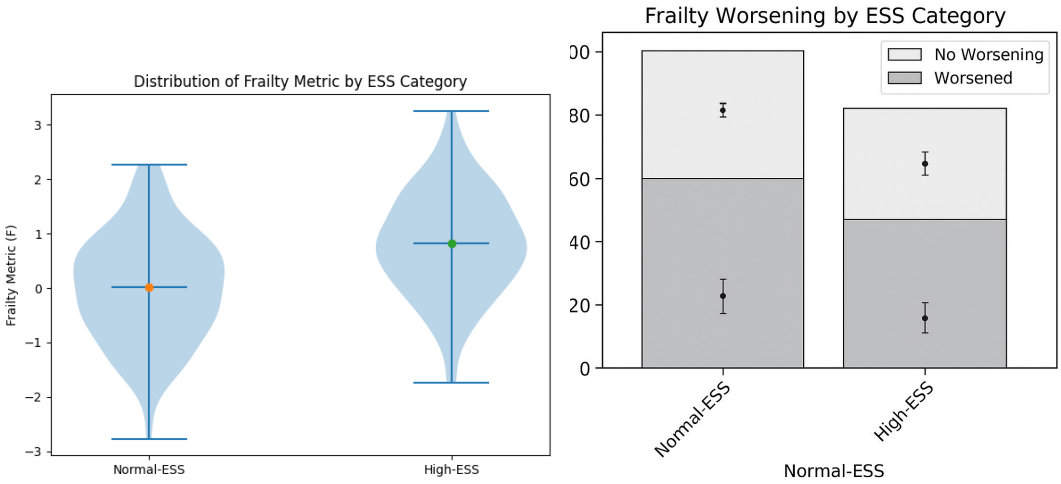
Distribution of the ΔFI by ESS



Note. Distribution of the frailty-related outcome (ΔFI) by ESS (Normal-ESS vs. High-ESS). Violin plots with median markers illustrate overlapping distributions. Mann-Whitney U = 5,692,277.50, Z = −0.362, p = .718.

Figure 2

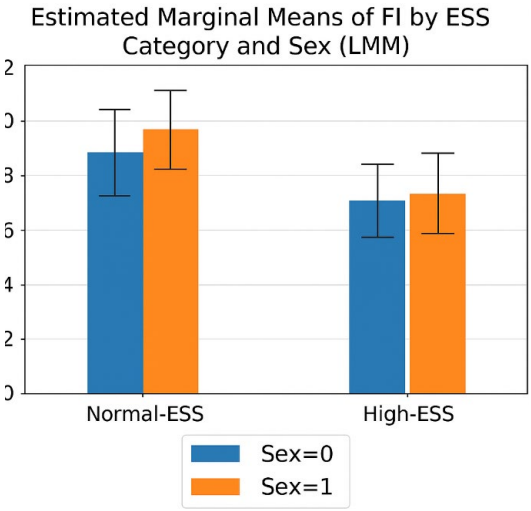
Frailty Worsening Proportions by ESS



Note. Proportion of veterans with FI_worth = 1 by ESS. High-ESS is associated with greater frailty worsening (19.5% vs. 16.8%), χ^2 (1, N = 6,824) = 8.14, p = .004; Phi = .035.

Figure 3

Estimated Marginal Means of Frailty Index by ESS And Sex



Note. Adjusted marginal means from the LMM for FI with covariates (age, BMI, CCI, time) held at sample means. ESS: Normal <11; High ≥11. Sex: 0=female, 1=male. Error bars = 95% CIs. Overlapping CIs indicate no ESS×sex interaction.

Discussion

This study examined the longitudinal association between sEDS, measured by the ESS, and frailty progression among veterans aged ≥50 years with diagnosed insomnia. Using national electronic health records and both linear mixed-effects and logistic models, sEDS was independently associated with a greater frailty burden and higher odds of frailty worsening after adjustment for age, BMI, CCI, and sex. Unadjusted analyses showed no group difference in ΔFI but a modestly higher proportion with frailty worsening in the High-ESS group (risk difference ≈2.7%), a small absolute effect that is nevertheless relevant at the population scale in the VHA. As expected in large observational cohorts, effect sizes were small, and adjusted models were needed to

account for confounding by age, adiposity, and multimorbidity; these models clarified an independent association between sEDS and higher frailty burden. Veterans with ESS ≥ 11 had consistently higher FI at baseline and at ~4-year follow-up relative to those with ESS < 11, and higher continuous ESS tracked with higher FI across time, reinforcing daytime sleepiness as a clinically useful marker of physiological vulnerability in older adults with chronic sleep disturbance (Çavuşoğlu et al., 2021; Sun et al., 2023). Importantly, the ESS×time interaction was not significant, indicating that sEDS marked a persistently higher frailty level rather than a faster rate of increase—i.e., a trait-like indicator of risk rather than a time-varying accelerator (Merlino et al., 2020; Newman et al., 2021; Ravyts & Dzierzewski, 2024; Sweetman, 2023). Logistic regression results converged with these findings: compared with ESS < 11, ESS ≥ 11 was associated with higher odds of frailty worsening, consistent with a dose–response pattern observed for continuous ESS in relation to FI (Wu et al., 2024; Zimmerman et al., 2024; Ribeiro et al., 2024; Soysal et al., 2021). Covariate patterns were epidemiologically coherent: higher BMI and male sex were linked to greater frailty burden and worsening, aligning with prior work on obesity, sex differences, and frailty risk (Mohajan & Mohajan, 2023; Bourassa et al., 2024). The inverse association of age and CCI with frailty worsening in adjusted logistic models likely reflects survivorship and selection dynamics in longitudinal EHR cohorts (Davison et al., 2020; Kang et al., 2024). Overall, these findings situate sEDS within a stress-process framework as a stable, quantifiable marker of elevated frailty risk in older veterans with insomnia and underscore the value of routine ESS screening and sleep-focused risk mitigation within veteran care (Hauri, 2021;

Byrne et al., 2021; Mooney, 2020; Al-Shargie et al., 2024; Zhang et al., 2024; Kaskirbayeva et al., 2023).

Implications

This work adds to evidence framing sleep disturbances as physiological stressors with downstream health consequences (Sun et al., 2023; Ravyts & Dzierzewski, 2024). Within the Stress Process Model, our findings support chronic subjective sleepiness as a trait-like marker of elevated frailty burden—an indicator consistent with biological aging vulnerability (Almeida, 2024; Fan et al., 2022)—rather than a driver of faster frailty accrual. Empirically, this study extends the limited longitudinal literature by demonstrating, in a large, real-world cohort of older veterans with insomnia, that higher ESS is independently associated with higher FI over ~4 years, with no ESS×time interaction, indicating a persistently higher frailty level (Byrne et al., 202we1; Merlino et al., 2020). Clinically, routine ESS screening can support early risk stratification: even small, adjusted effects at the individual level translate into meaningful population impact in the VHA, where sleep disturbance is common. Because ESS is already embedded in practice, incorporating ESS (both continuous scores and the ≥11 threshold) into geriatric assessments and EHR-based prompts is a low-cost, scalable step to flag patients for closer evaluation and multimodal management (Zimmerman et al., 2024; Soysal et al., 2021; Hauri, 2021; Mysliwiec et al., 2020). While this study did not test treatments, existing guidance support offering CBT-I, assessing for and treating sleep-disordered breathing (e.g., CPAP when indicated), and addressing modifiable risks (physical activity, weight management, medication review) as part of comprehensive frailty

mitigation (Sweetman, 2023; Kansagra, 2020). At the system level, prioritizing sleep health in aging veterans, through improved access to diagnostics, behavioral interventions, and coordinated geriatric-sleep pathways, may promote healthy aging, reduce hospitalization, and enhance quality of life (Mooney, 2020; Davison et al., 2020; Newman et al., 2021; Henrique et al., 2023). At the individual and family levels, addressing daytime sleepiness with behavioral and medical strategies may help preserve independence and lessen caregiver burden, complementing broader efforts to slow functional decline (Whitty et al., 2020; Ravyts & Dzierzewski, 2024).

Recommendations for Future Research

Building on these findings and limitations, future work should employ prospective, multiwave designs with more frequent FI assessments to capture nonlinear and dynamic frailty trajectories and to separate level effects from slope (Kaskirbayeva et al., 2023; Minici, 2023). Serial measurement of ESS (and objective sleep metrics where feasible) would enable within-person analyses of change in sleepiness versus baseline status and clarify whether shifts in sEDS map onto subsequent frailty shifts (Zhang et al., 2024; Al-Shargie et al., 2024). To enhance generalizability and equity, samples should intentionally include female veterans and civilian cohorts, with prespecified subgroup analyses by sex, race/ethnicity, and service era/PTSD status (Byrne et al., 2021; Kang et al., 2024; Bourassa et al., 2024). Etiologic models should incorporate additional psychological (e.g., depression, PTSD), behavioral (e.g., physical activity), and physiological markers (e.g., inflammatory indices) to test mechanisms linking sEDS to frailty via mediation and to address time-varying confounding using modern causal

methods (e.g., IPTW/MSMs) and robust handling of survivorship/attrition (Zhang et al., 2024; Al-Shargie et al., 2024; Bourassa et al., 2024). Finally, intervention studies, including randomized and pragmatic trials, should evaluate whether sleep-targeted treatments (e.g., CBT-I, CPAP where indicated, multimodal programs) reduce frailty burden and worsening, with careful attention to adherence, dose, and patient-reported outcomes to support translation into routine VHA care (Sweetman, 2023; Sun et al., 2023).

Conclusion

SEDS, indexed by the ESS, was independently associated with a greater frailty burden and higher odds of frailty worsening over ~4 years among veterans aged ≥50 years with insomnia (Fan et al., 2022; Soysal et al., 2021). Linear mixed models showed no ESS×time interaction, indicating that sEDS marks a persistently higher level of frailty rather than a faster rate of increase—supporting its role as a stable, clinically meaningful indicator of physiological vulnerability (Merlino et al., 2020; Newman et al., 2021). These convergent findings, including dose–response patterns for ESS, reinforce sEDS as a practical screening target in geriatric sleep care (Wu et al., 2024; Ribeiro et al., 2024). Integrating routine ESS assessment into veteran health system workflows can facilitate early risk stratification and timely, multimodal management, such as evaluation for sleep-disordered breathing, referral to CBT-I, activity/weight optimization, and medication review, to help preserve function and quality of life in aging veterans (Mysliwiec et al., 2020; Whitty et al., 2020).

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Association Between Medical Interventions and Frailty Progression in Veterans with Insomnia and Abnormal ESS Scores

Mona Amirmazaheri

Department of Public Health, Walden University

Supported by the Department of Veteran Affairs, Michael E. De Bakey VA Medical Center (MEDVAMC), Baylor College of Medicine (BCM)

All findings and conclusions are solely those of the authors.

Outlet for Manuscript

Journal of Clinical Sleep Medicine (JCSM) is a strong fit for *"Association Between Medical Interventions and Frailty Progression in Veterans with Insomnia and Abnormal ESS Scores."* The paper delivers clinically actionable evidence on how common sleep treatments, CBT-I, CPAP, and prescription sleep medication, relate to frailty in older adults, using a large, real-world VHA cohort and validated outcomes (Frailty Index, ESS). Its retrospective longitudinal design with linear mixed models and adjusted logistic regression, clear reporting of effect sizes/95% CIs, and emphasis on treatment implications align with JCSM's clinical mission and AMA style expectations (structured abstract; standard medical terminology; AMA-formatted references, tables, and figures). The focus on an older veteran population with multimorbidity and insomnia extends JCSM's readership interests in translating sleep interventions into measurable health benefits, informing guideline refinement and care pathways in geriatric sleep medicine.

Key words: Cognitive Behavioral Therapy for Insomnia (CBT-I); Continuous Positive Airway Pressure (CPAP); Epworth Sleepiness Scale (ESS); Frailty Index; Insomnia; Veterans

Highlights:

Large VHA cohort (N=6,824; ≥50y with insomnia, abnormal ESS): FI measured at baseline and ~4-year follow-up; LMM and adjusted logistic models used.

Intervention effects: CBT-I (aOR≈0.31, 95% CI 0.19–0.53) and CPAP (aOR≈0.55, 95% CI 0.39–0.76) associated with lower odds of frailty worsening;

prescription sleep medication associated with higher odds (aOR≈1.16, 95% CI 1.02–1.32).

Trajectories: LMM showed lower predicted FI over time with CBT-I/CPAP and higher FI with medication use.

Clinical takeaway: Prioritize nonpharmacologic sleep care (CBT-I, CPAP when indicated) for older veterans with insomnia and daytime sleepiness; use pharmacotherapy judiciously.

Abstract

Frailty progression is a major concern in older veterans with insomnia and sEDS. I examined whether commonly used sleep interventions, prescription sleep medication, cognitive behavioral therapy for insomnia (CBT-I), and continuous positive airway pressure (CPAP) are associated with frailty outcomes in this population. In a retrospective cohort using Veterans Health Administration corporate data warehouse electronic medical records (2019–2023), participants included veterans aged ≥50 years with an insomnia diagnosis and a documented Epworth sleepiness scale (ESS; abnormal ESS defined as ≥11). Frailty was quantified by the frailty index (FI) at baseline and approximately 4-year follow-up. Associations between interventions and frailty were evaluated using linear mixed models for FI trajectories and multivariable logistic regression for frailty worsening (FI_worsen=1), adjusting for age, sex, BMI, CCI, and race. Among 6,824 veterans, 18.0% experienced frailty worsening over 4 years. In adjusted models, sleep medication use was associated with higher odds of frailty worsening (adjusted odds ratio [aOR] 1.16, 95% CI 1.02–1.32), whereas CBT-I (aOR 0.31, 95% CI 0.19–0.53) and CPAP (aOR 0.55, 95% CI 0.39–0.76) were associated with lower odds. Linear mixed model findings were directionally consistent: medication exposure corresponded to higher FI across time, while CBT-I and CPAP corresponded to lower FI. Male sex and higher body mass index were associated with greater frailty burden; patterns for age and comorbidity suggested possible survivorship or treatment-selection effects. These results support prioritizing nonpharmacologic and OSA-targeted

strategies (CBT-I, CPAP) to mitigate frailty risk in older veterans with insomnia and abnormal ESS.

Introduction

Problem Focus

The high prevalence of sleep disorders among aging veterans is considered a significant health challenge, particularly in the presence of insomnia and subjective excessive daytime sleepiness (sEDS). Veterans aged 50 and older are at increased risk for the adverse effects of sleep disturbances, which may be associated with frailty, a multidimensional syndrome characterized by decreased physiological reserve and increased vulnerability to adverse health outcomes. This manuscript examines the association between medical interventions, including prescribed sleep medications RXs, cognitive behavioral therapy for insomnia (CBT-I), and continuous positive airway pressure (CPAP), and frailty progression in veterans with insomnia and abnormal ESS scores. Despite the widespread use of these interventions, their long-term relationship with frailty progression in this high-risk population remains insufficiently studied, highlighting a critical gap in clinical research and practice

Significance/Importance

This research has critical implications for sleep medicine, geriatric care, and veteran health. Given the aging veteran population, evaluating the association between sleep interventions and frailty progression is essential for improving patient outcomes and reducing healthcare system burdens. Frailty is associated with increased risks of falls, hospitalization, disability, and mortality, emphasizing the need for effective management

strategies in older adults. By analyzing the effectiveness of sleep-related medical interventions, this study provides empirical data on frailty progression in older veterans. The findings contribute to public health efforts aimed at developing targeted interventions for aging populations.

Theoretical Framework

This study applies the clinical epidemiology framework, which integrates epidemiological principles into clinical practice to assess patient care outcomes. This framework is well-suited for evaluating the real-world effectiveness of medical interventions in managing frailty progression. By analyzing the patterns, determinants, and outcomes of sleep interventions in a defined clinical population, this study generates evidence-based insights to support clinical decision-making. Additionally, the clinical epidemiology framework facilitates the identification of risk factors and the development of prognostic models, which are essential for optimizing treatment strategies in geriatric care.

Contributions and Purpose of Research

This study provides a quantitative assessment of the intersection between sleep medicine and geriatric health in the veteran care context. Addressing a gap in the literature, it examines the quantitative association between medical interventions, including sleep medications, CBT-I, and CPAP, on frailty progression in veterans aged 50 and older with insomnia and abnormal ESS scores. By providing adequate evidence on the effectiveness of these interventions, the study informs clinical guidelines and treatment strategies aimed at optimizing health outcomes for older veterans. This focus is

particularly relevant given the increasing prevalence of sleep disorders and frailty in aging veterans, highlighting the need for targeted, evidence-based healthcare strategies. Through the clinical epidemiology framework, the findings contribute to recognizing risk factors and prognostic model development, supporting the implementation of interventions designed to slow or mitigate frailty progression. The results are aligned with broader public health objectives to improve the quality of life in this high-risk population.

Relevant Scholarship

Existing research on sleep disorders and frailty examines the complex and bidirectional association between these conditions, both of which are highly prevalent in older adults, including veterans. Sleep disorders, such as insomnia and sEDS, have been extensively studied in geriatric populations due to their association with adverse health outcomes (Keil et al., 2023; Kim et al., 2022). These outcomes include cognitive decline, reduced physical mobility, an elevated risk of falls, and increased mortality (Merlino et al., 2020). Despite extensive research on these associations, limited evidence is available on the long-term effects of medical interventions for sleep disorders on frailty progression (Merlino et al., 2020). Sleep disorders, including insomnia and sEDS, are highly prevalent among older adults, affecting approximately 30-50% of the aging population (Bjornsdottir et al., 2024). The prevalence is even higher among veterans due to comorbidities, PTSD, chronic pain, and the long-term impact of military service. Insomnia, characterized by difficulty initiating or maintaining sleep or the inability to achieve restorative sleep, is associated with cognitive and physical impairments

(Bourassa et al., 2024; Byrne et al., 2021). Epidemiology studies have shown that individuals with insomnia have higher risks of developing cardiovascular diseases, metabolic disorders, and neurodegenerative conditions such as Alzheimer's disease (Bjornsdottir et al., 2024). SEDS, often quantified using ESS, is another prevalent sleep disorder in older adults, and is associated with a higher likelihood of accidents, reduced work productivity, and overall lower quality of life (Walker et al., 2020). Both insomnia and sEDS contribute to declining physical health and may contribute to frailty progression, a geriatric syndrome characterized by reduced physiological reserve and increased susceptibility to stressors like illness and injury (Hofman et al., 2022).

CBT-I and CPAP are among the most extensively studied interventions for managing sleep disorders in older adults (Aboussouan et al., 2023; El Basiouny & Habib, 2023). CBT-I is a structured, evidence-based treatment that incorporates strategies such as stimulus control, sleep restriction, cognitive restructuring, and sleep hygiene improvements (El Basiouny & Habib, 2023). It can be delivered in both individual and group therapy settings. As the first-line treatment for chronic insomnia, CBT-I addresses the cognitive and behavioral factors that sustain sleep difficulties (El Basiouny & Habib, 2023). Randomized controlled trials (RCTs) have shown their effectiveness in enhancing sleep quality, reducing nighttime awakenings, and improving overall sleep efficiency, supporting its role as a highly effective nonpharmacological treatment for insomnia (El Basiouny & Habib, 2023). CBT-I is designed to modify maladaptive sleep-related beliefs, enhance sleep hygiene practices, and incorporate relaxation techniques to reduce pre-sleep anxiety (El Basiouny & Habib, 2023). CPAP therapy, the standard treatment for

obstructive sleep apnea (OSA), is effective in maintaining airway patients, preventing apnea episodes, and improving oxygen saturation during sleep. OSA frequently co-exists with insomnia and sEDS, and studies have shown that CPAP therapy improves daytime alertness and reduces the cardiovascular risks associated with sleep apnea (Aboussouan et al., 2023).

However, existing literature primarily examines the short-term effects of both therapies, focusing on sleep quality and daytime functioning. Limited evidence is available on the long-term associations between these interventions and broader health outcomes, particularly frailty (Alqahtani, 2021). Despite the established effectiveness of CBT-I and CPAP in managing sleep disorders, limited research has examined their long-term association with frailty progression. Frailty, characterized by physical impairments such as decreased strength, reduced walking speed, and lower physical activity levels, serves as a key indicator of aging (Xu et al., 2024). It is a strong predictor of adverse health outcomes, including falls, hospitalization, and mortality (Piovezan et al., 2023). While improvements in sleep quality may help mitigate physiological stressors associated with frailty, the direct association between sleep interventions and frailty progression or reversal remains insufficiently studied (Pourmotabbed et al., 2020; Wen et al., 2023). Limited research has examined the association between sleep interventions and frailty. A small study on CPAP uses in older adults with OSA reported improvements in physical activity levels and self-reported physical function (Xue et al., 2024). Similarly, preliminary evidence indicates that CBT-I is associated with a reduced risk of falls in frail older adults through improvements in sleep quality and cognitive function. However,

existing studies are limited by short follow-up periods and small sample sizes, resulting in insufficient data on the long-term effects of these interventions on frailty progression (Wang et al., 2024). Veterans, aged 50 and older, represent a distinct patient population due to the cumulative effects of military service, including chronic pain, PTSD, and exposure to traumatic events. These factors are associated with a higher prevalence of sleep disorders and may contribute to frailty progression (Bourassa et al., 2024). For example, veterans have an increased risk of PTSD-related insomnia, which is associated with chronic stress, inflammation, and frailty (Simon et al., 2024). Despite the high prevalence of both sleep disorders and frailty in this population, limited research has specifically examined the long-term effects of targeted sleep interventions in veterans (Simon et al., 2024). The VHA maintains extensive healthcare data on veterans, providing an opportunity for the experts to explore long-term outcomes of sleep interventions in a high-risk, aging population (DeBellis et al., 2023). However, limited research has utilized these data to assess the associations between CBT-I or CPAP use and frailty progression in veterans. The gap is notable, as veterans' health profiles differ from the general population due to unique service-related exposures and comorbidities. This study addresses a notable gap in literature by conducting a longitudinal analysis of the associations between sleep medication, CBT-I, and CPAP therapy with frailty progression in older veterans. While these interventions are well-established treatments for sleep disorders, their long-term associations with frailty, a key predictor of health outcomes and longevity in aging populations, remain insufficiently studied. Existing research primarily examines the short-term effects of sleep interventions on sleep quality

and daytime functioning, with limited studies evaluating their broader associations with physical function, physiological resilience, and overall health outcomes in older adults. Utilizing a large data set from the Veterans Health Administration (VHA), this study can provide empirical evidence on whether improving sleep quality through these interventions is associated with reductions in frailty risk among veterans.

Research Questions and Design

The central research question for this study is: What is the association between medical interventions (sleep medication, CBT-I, and CPAP) and frailty progression among veterans aged 50 and older with insomnia and abnormal ESS scores, after controlling for age, sex, BMI, and CCI?

In this study, I evaluate the association between specific medical interventions and frailty progression in older veterans, a population with a higher prevalence of sleep disorders and frailty due to the physiological and psychological effects of military service. Previous studies have established an association between sleep disorders and adverse health outcomes, including frailty; however, limited evidence is available regarding the long-term associations between using medical interventions and frailty progression. Evaluating the associations between these medical interventions and frailty progression is essential for developing targeted treatment strategies to improve health outcomes and quality of life in this population. This study addresses a notable gap in the literature by providing empirical evidence on the effectiveness of these interventions.

Also, within the study, I examine whether these treatments not only address the immediate symptoms of sleep disorders but also have long-term associations with health

outcomes such as frailty. Assessing this relationship provides evidence of the potential role of sleep interventions in managing or slowing frailty progression in aging veterans. To investigate this association, the study employs a retrospective cohort design, utilizing data from the VHA electronic medical records (EMRs). This study design facilitates the examination of long-term health outcomes in a large, well-defined population. The analysis includes veterans aged 50 and older diagnosed with insomnia and presenting with abnormal ESS scores (indicative of EDS). The primary objective is to quantitatively assess the associations between sleep medication, CBT-I, and CPAP therapy and frailty progression over time, with frailty measured using the FI. The analysis controls for confounders, age, sex, BMI, and CCI, to account for potential confounders and ensure that observed associations reflect the effects of these interventions rather than underlying factors. This retrospective cohort design is well-suited and used to analyze real-world data over an extended period, providing evidence on the long-term effects of these interventions on frailty. The inclusion of a large and diverse veteran population strengthens the generalizability of the findings, making them relevant to a broader clinical setting. Additionally, rigorous statistical methods are employed to adjust for key demographic and health-related variables, ensuring that the results are robust, reliable, and applicable to clinical practice and policy development in sleep medicine and geriatric care. The research question and study design are structured to examine the associations between sleep interventions and frailty progression in older veterans. This study provides empirical data to support the development of clinical management strategies for this high-

risk population. The findings may inform future treatment guidelines and optimize care strategies for veterans with sleep disorders and frailty.

Methods

Study Approval and Data Source

This retrospective cohort study was conducted with approval from the Institutional Review Board (IRB) of Walden University, Baylor College of Medicine (BCM), and the Research and Development (R&D) Committee of the Michael E. DeBakey VA Medical Center (MEDVAMC). The study utilized EMRs from the VHA corporate data warehouse (CDW), a nationally integrated relational database that aggregates patient data from all VHA facilities across the United States. The data set includes records from 2019 to 2023, encompassing both inpatient and outpatient encounters, along with diagnoses, prescribed medications, laboratory results, vital signs, and physician notes. The CDW data set was structured to evaluate associations between insomnia, sEDS, frailty progression, and treatment interventions among older veterans. Its relational database structure allows for the integration of multiple data sources, supporting longitudinal analyses of sleep disorders and frailty. The availability of comprehensive demographic, clinical, and treatment data facilitates an in-depth assessment of these associations while accounting for key medical, psychological, and demographic variables.

Cohort Selection

The study cohort included 6,824 veterans aged 50 years and older who met the inclusion criteria. All participants had a diagnosis of insomnia and documented ESS

scores. The cohort was stratified into two groups based on ESS scores: 3,859 veterans with normal daytime sleepiness (ESS ≤ 10) and 2,965 veterans with abnormal daytime sleepiness (ESS ≥ 11). Participants' selection was based on their receipt of care within the VHA system and their exposure to sleep-related medical interventions, including sleep medication, CBT-I, or CPAP therapy. Veterans with incomplete or missing ESS scores, or those who had not received any of the specified interventions, were excluded from the analysis. A priori power analysis was conducted to assess the adequacy of the sample size, incorporating expected effect sizes, an alpha level of 0.05, and a desired statistical power of 0.80. The results indicated that the sample size was sufficient to detect statistically significant associations between the interventions and frailty progression.

Additionally, the large cohort size facilitated subgroup analyses to assess the associations between sleep interventions and frailty progression across subpopulations stratified by comorbidity burden and demographic characteristics. This analysis enhances the statistical rigor of the study and ensures robust and reliable estimates of the association between sleep-related interventions and frailty progression in older veterans.

Variables and Data Sources

The primary exposure variables in this study are sleep-related medical interventions documented in the VHA EMRs. These interventions include prescribed sleep medications as part of the veterans' treatment plans for managing sleep disorders. Additionally, CBT-I was utilized as a therapeutic intervention for insomnia symptoms, while CPAP therapy was prescribed for veterans with comorbid sleep apnea (OSA).

These interventions are examined to assess their associations with frailty progression. The analysis accounts for potential confounders to ensure that observed relationships reflect the effects of these interventions rather than underlying health conditions. The outcome variable for this study is frailty progression, measured through changes in the frailty index (FI) over 4 years. FI was measured at two-time points—baseline (corresponding to the time of insomnia diagnosis) and 4 years post-baseline. This index quantifies frailty by assessing the accumulation of health deficits across physical, cognitive, and functional domains, facilitating an evaluation of frailty progression over time with sleep-related medical.

Control variables included demographic factors; age, sex, race, and ethnicity, as well as BMI and CCI. Age was calculated based on date of birth at baseline, while sex was categorized as male or female. BMI was derived from height and weight measurements recorded near the baseline, providing an indicator of body composition. CCI was used to quantify comorbidity burden, calculated based on chronic health conditions documented in the year preceding insomnia diagnosis. Race and ethnicity were recorded as categorical variables in the EMRs to account for demographic influences on health outcomes. These control variables were incorporated to adjust for potential confounding and ensure that observed associations between sleep interventions and frailty progression were not attributable to underlying demographic or clinical differences.

Instrumentation and Measures

ESS is a validated self-reported questionnaire used to measure daytime sleepiness by assessing the likelihood of dozing off in various daily situations. The ESS consists of eight items, each rated on a 4-point scale (0–3), yielding a total score ranging from 0 to 24. Higher scores indicate greater levels of daytime sleepiness, with an ESS score of ≥11 operationally defining EDS. In this study, ESS scores were extracted from unstructured clinical notes using a validated natural language processing (NLP) algorithm to enhance accuracy and consistency in identifying sEDS.

Frailty progression, the primary outcome measure in this study, is assessed by quantifying changes in the FI from baseline to follow-up. The concept of *frailty worth* is applied to categorize these changes, calculated as the difference between the follow-up FI (FI_final) and the baseline FI (FI0). Frailty worth is classified into two categories to reflect changes in health status over time: No worsening of frailty, indicating stable or improved health status (0); and Worsened frailty status, indicating a decline in health (1). This classification facilitates a targeted analysis of frailty progression, with a focus on individuals who experienced frailty during the study period (Kaskirbayeva et al., 2023). FI serves as a quantitative measure of frailty, calculated based on the accumulation of health deficits. These deficits included comorbidities, disabilities, and functional impairments, with each deficit assigned a value of 0 (absent) or 1 (present). The total number of deficits is divided by the total number of potential deficits to produce an FI score ranging from 0 (no frailty) to 1 (complete frailty). Higher FI scores indicate greater frailty severity. The FI provided a comprehensive assessment of physiological

vulnerability to adverse health outcomes and was essential for evaluating frailty progression over the study period. Health status is evaluated using the Charlson comorbidity index (CCI), a validated measure for quantifying comorbidity burden and estimating mortality risk. The CCI ranges from 1 to 27, incorporating both the number and severity of chronic health conditions. For statistical analysis, the CCI is categorized into low comorbidity (CCI 0–1) and high comorbidity (CCI ≥2) (Kachlíková et al., 2020). This index is broadly used in epidemiological research to adjust for the potential confounding effects of comorbidities on health outcomes. In this study, the CCI was included as a covariate to account for baseline differences in comorbidity burden. This adjustment helped ensure that associations between sleep interventions, sEDS, and frailty progression were analyzed independent of pre-existing chronic conditions. These measures were based on their validated use in clinical and epidemiological research. Collectively, they establish a systematic approach for assessing the associations between sleep disorders and sleep-related interventions and health outcomes in an aging veteran population.

Statistical Analysis Strategies

In this study, a retrospective cohort design has been used to examine the longitudinal associations between medical interventions and frailty progression. The design allows for the analysis of existing EMR data, from a large population over an extended follow-up period. The retrospective cohort design was selected based on its capacity to leverage comprehensive, preexisting clinical data to assess temporal relationships between medical interventions and health outcomes. This methodology

facilitates the identification of associations and supports the evaluation of potential causal links between sleep-related treatments and frailty progression.

Statistical Analysis

Descriptive statistics: Baseline characteristics of the study population were summarized using descriptive statistics, including demographic variables (age, sex, race, and ethnicity), ESS scores, and the types of sleep-related medical interventions received (sleep medication, CBT-I, and CPAP therapy). The distribution of FI scores at baseline and the 4-year follow-up were reported to describe frailty progression over time. Measures of central tendency (mean or median) and dispersion (standard deviation or interquartile range) were presented as appropriate for data distribution. Multivariable Logistic Regression: The association between medical interventions (exposure variables) and frailty progression (outcome variable) were examined using multivariable logistic regression models. These models adjust for potential confounders, including age, sex, BMI, race, ethnicity, and CCI, to estimate the independent effect of each intervention. Adjusted odds ratios (aOR) with 95% confidence intervals (95% CI) were calculated to quantify the strength and direction of these associations. Statistical significance was evaluated using a p-value threshold of 0.05. Linear Mixed Models (LMM) were also employed to analyze the longitudinal effects of sleep-related medical interventions on frailty progression. LMMs provide a robust analytical framework for evaluating repeated measures while accounting for the correlated structure of longitudinal data. This approach accommodates variability across individuals, controls confounding factors, and manages missing data within the study population. LMMs enable a precise estimation of how

medical interventions influence frailty trajectories over time while adjusting for relevant covariates. The combination of a retrospective cohort design and advanced statistical techniques allows for a rigorous assessment of the associations between sleep-related medical interventions and frailty progression. The study's large sample size and comprehensive electronic health record data from the VHA strengthen the statistical power and generalizability of the findings. This methodological approach enhances internal validity and reliability, ensuring that the results contribute to evidence-based clinical decision-making aimed at optimizing health outcomes for older veterans with insomnia.

Results

I analyzed 6,824 veterans aged ≥50 years with insomnia and available ESS. Mean (SD) age was 61.79 (7.82) years (range 50–97), BMI 31.47 (5.92) kg/m², and CCI 1.41 (1.84). By category, 66.4% were 50–65 and 33.6% were >65; 90.6% were male. Race/ethnicity was 70.5% White, 21.5% Black, 8.0% other, and 7.2% Hispanic. PTSD was documented in 35.2%. Obesity (BMI ≥30) was present in 56.3% and CCI ≥2 in 33.4%. ESS ≥11 occurred in 43.4%. At baseline (FI_0), 65.2% were robust, 23.8% pre-frail, and 11.0% frail; at ~4-year follow-up, 62.0% were robust, 22.0% pre-frail, and 16.0% frail. Frailty worsening (FI_worsen=1) occurred in 18.0%. Sleep-related interventions were sleeping medication 53.3%, CBT-I 3.3%, and CPAP 3.2%. Full baseline characteristics and cross-tabulations are provided in Table 1. I fit a multivariable logistic regression to assess associations between sleep interventions and frailty worsening (FI_worsen=1 vs 0). Exposures were prescription sleep medication (Rx),

CBT-I, and CPAP; covariates were age, sex, BMI, CCI, and race. The analysis included 6,824 complete cases; no variables were excluded for multicollinearity or sparse data. Model fit was adequate (Hosmer–Lemeshow χ^2 (8) =13.49, p=.096; Nagelkerke R^2=0.042). In adjusted estimates, Rx was associated with higher odds of frailty worsening (aOR 1.16, 95% CI 1.02–1.32), whereas CBT-I (aOR 0.31, 95% CI 0.19–0.53) and CPAP (aOR 0.55, 95% CI 0.39–0.76) were associated with lower odds. Full coefficients and adjusted associations are summarized in Table 2. Prescription sleep medication (Rx) was associated with higher odds of frailty worsening (aOR 1.158, 95% CI 1.020–1.315). CBT-I (aOR 0.314, 95% CI 0.186–0.530) and CPAP (aOR 0.546, 95% CI 0.394–0.758) were associated with lower odds. Among covariates, age was inversely associated (aOR 0.980, 95% CI 0.972–0.989), male sex was positively associated (aOR 1.762, 95% CI 1.379–2.251), BMI showed a small positive association (aOR 1.030, 95% CI 1.019–1.040), CCI showed an inverse association (aOR 0.873, 95% CI 0.837–0.910), and non-White race was associated with lower odds relative to the reference (aOR 0.882, 95% CI 0.794–0.979). Figure 2 displays a forest plot of adjusted aORs (95% CIs) from the multivariable model for Rx, CBT-I, CPAP, and covariates; numerical estimates correspond to Table 2.

I modeled FI at baseline and ~4-year follow-up using a linear mixed model with random intercepts (participant as the clustering unit) and time (0, 4 years) as a repeated factor. Fixed effects included sleep interventions (prescription sleep medication Rx, CBT-I, CPAP), ESS (continuous), age, sex, race, BMI, and CCI, plus intervention×time interactions. All 6,824 participants contributed 13,648 observations. An unstructured

covariance was specified; models were estimated by REML with Satterthwaite degrees of freedom. Overall fit was adequate (AIC ≈ −30,830; BIC ≈ −30,800). In adjusted analyses (Table 3), Rx was associated with higher FI across time (p<.001). CBT-I was associated with lower FI across time (p=.009). CPAP showed no significant main effect (p=.465), but the CPAP×time interaction was significant (p=.022), indicating differential change over follow-up. No other intervention×time interactions reached significance. Among covariates, ESS was positively associated with FI (≈0.001 FI units per ESS point; p<.001). BMI and CCI were positively associated with FI (both p<.001). Age showed a small inverse association (p=.003). Effects for sex and race were modest (see Table 3 for estimates, 95% CIs, and full model coefficients).

Figure 3. Predicted FI trajectories by intervention status. Model-based predicted FI (±95% CI) at baseline and ~4-year follow-up are shown with covariates held at sample means. Veterans receiving prescription sleep medication (Rx) had higher FI at both time points; the Rx×time interaction was not significant. CBT-I was associated with lower FI and a significant CBT-I×time interaction, indicating differential change over follow-up. CPAP showed no significant main effect, but the CPAP×time interaction was significant. Numerical estimates and p-values appear in Table 3.

Figure 4. Fixed effect estimates with 95% CIs. Forest plot of adjusted linear mixed model coefficients (β, 95% CI) for interventions and covariates. Rx was positively associated with FI; CBT-I was negatively associated; CPAP×time and CBT-I×time were significant. Among covariates, ESS, BMI, and CCI were positively associated with FI,

whereas age showed a small inverse association; effects for sex and race were modest. Full estimates are reported in Table 3.

Table 1

Descriptive Results: Demographic, Clinical, and Treatment

Category		n (%)
Age M (SD) = 61.79 (7.82)	50–65 >65	4,531 (66.4%) 2293 (33.6%)
Sex	Male Female	6,184 (90.6%) 640 (9.4%)
Race	White Black Other	4,811 (70.5%) 1,470 (21.5%) 543 (8.0%)
Ethnicity	Non-Hispanic Hispanic	6,335 (92.8%) 489 (7.2%)
BMI M (SD) = 31.47 (5.92)	<30 (non-obese) ≥30 (obese)	2,984 (43.7%) 3,840 (56.3%)
CCI Category M (SD) = 1.41 (1.84)	Low (0–1) High (≥2)	4,547 (66.6%) 2,277 (33.4%)
PTSD Diagnosis	Yes No	2,389 (35.2%) 4,399 (64.8%)
ESS	Normal (≤10) Abnormal (≥11)	3,859 (56.6%) 2,965 (43.4%)
Frailty (Baseline)	Robust Pre-frail Frail	4,448 (65.2%) 1,626 (23.8%) 750 (11.0%)
Frailty (Follow-up)	Robust Pre-frail Frail	4,232 (62.0%) 1,500 (22.0%) 1,092 (16.0%)
Frailty Progression (FI_worth)	No Worsening Worsening	5,597 (82.0%) 1,227 (18.0%)
Sleep Medication (Rx)	Yes No	3,636 (53.3%) 3,188 (46.7%)
CBT-I	Yes No	226 (3.3%) 6,598 (96.7%)
CPAP	Yes No	221 (3.2%) 6,603 (96.8%)

Note. BMI = Body Mass Index; CCI = Charlson Comorbidity Index; PTSD = posttraumatic stress disorder; ESS = Epworth Sleepiness Scale; FI = Frailty Index; CBT-I

= Cognitive Behavioral Therapy for Insomnia; CPAP = Continuous Positive Airway Pressure.

Table 2

Logistic Regression Predicting Odds of Frailty Progression

Predictor	B	SE	Wald	df	p	aOR	95% XI
Rx	0.147	0.065	5.15	1	.023	1.158	[1.020, 1.315]
CBT-I	-1.159	0.268	18.74	1	<.001	0.314	[0.186, 0.530]
CPAP	-0.605	0.167	13.12	1	<.001	0.546	[0.394, 0.758]
Age	-0.020	0.005	18.90	1	<.001	0.980	[0.972, 0.989]
Sex (Male)	0.566	0.125	20.52	1	<.001	1.762	[1.379, 2.251]
CCI	-0.136	0.021	40.91	1	<.001	0.873	[0.837, 0.910]
BMI	0.029	0.005	29.74	1	<.001	1.030	[1.019, 1.040]
Race (Non-White)	-0.126	0.053	5.55	1	.019	0.882	[0.794, 0.979]
Constant	-0.872	0.398	4.80	1	.028	0.418	—

Note. N = 6,824. aOR = adjusted odds ratio; FI_worth = frailty progression. Rx = sleep medication; All covariates were adjusted in the model

Table 3

Fixed Effects from Linear Mixed Model

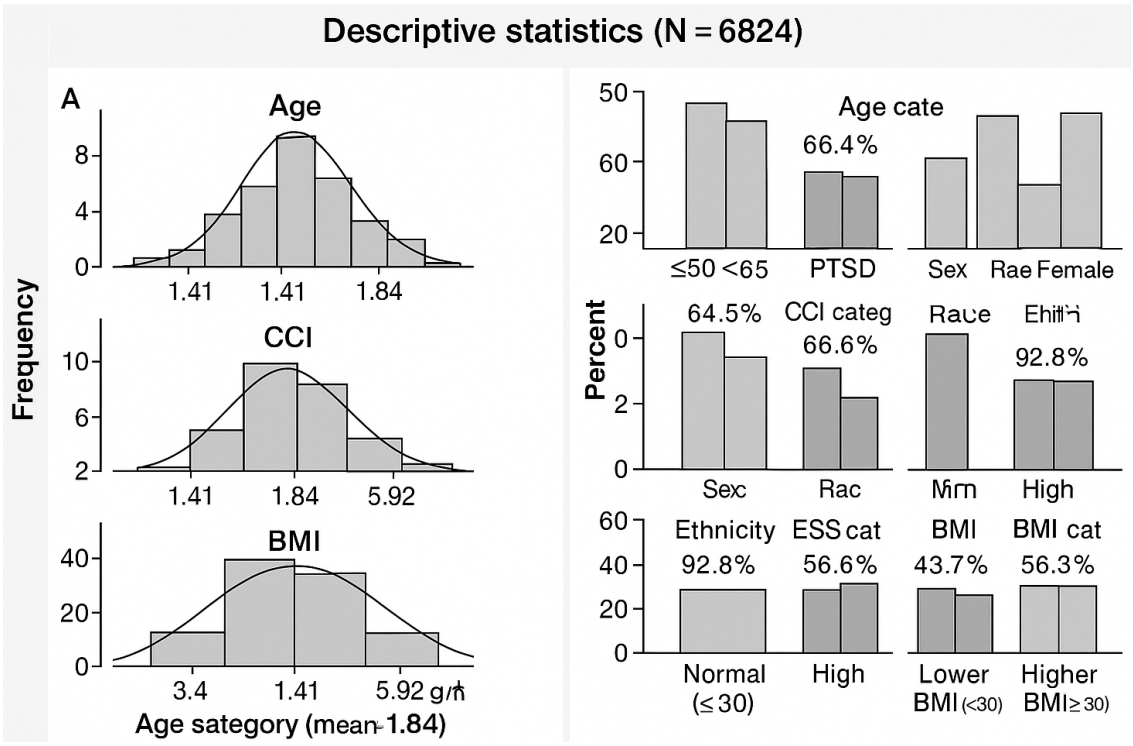
Predictor	Estimate (B)	SE	df	t	p
Intercept	0.033	0.013	7001	2.577	0.010
Time	0.002	0.001	6820	1.542	0.123
Rx	-0.019	0.002	6830	-8.974	0.000
CBT-I	0.016	0.006	6814	2.621	0.009
CPAP	0.004	0.006	6819	0.731	0.465

Sex (Male)	-0.011	0.004	6813	-3.103	0.002
Race (Black)	0.017	0.004	6812	4.415	0.000
Race (Other)	0.006	0.004	6814	1.313	0.189
ESS	0.001	0.000	6812	5.628	0.000
CCI	0.01	0.001	6816	16.853	0.000
Age	0.000	0.000	6810	-2.951	0.003
BMI	0.001	0.000	6814	7.776	0.000
Rx_cat2 × Time	0.000	0.001	6826	0.534	0.593
CBT-I × Time	0.003	0.001	6820	2.107	0.035
CPAP × Time	0.003	0.001	6820	2.284	0.022

Note. Fixed effects from an LMM of FI over time. Predictors: time (years), interventions (Rx, CBT-I, CPAP), demographics (age, sex, race), and clinical covariates (BMI, ESS, CCI). Interaction terms indicate differential change by intervention across 4 years. B = unstandardized coefficient; SE = standard error; df = degrees of freedom; p = two-tailed. Bold = $p<.05$

Figure 1

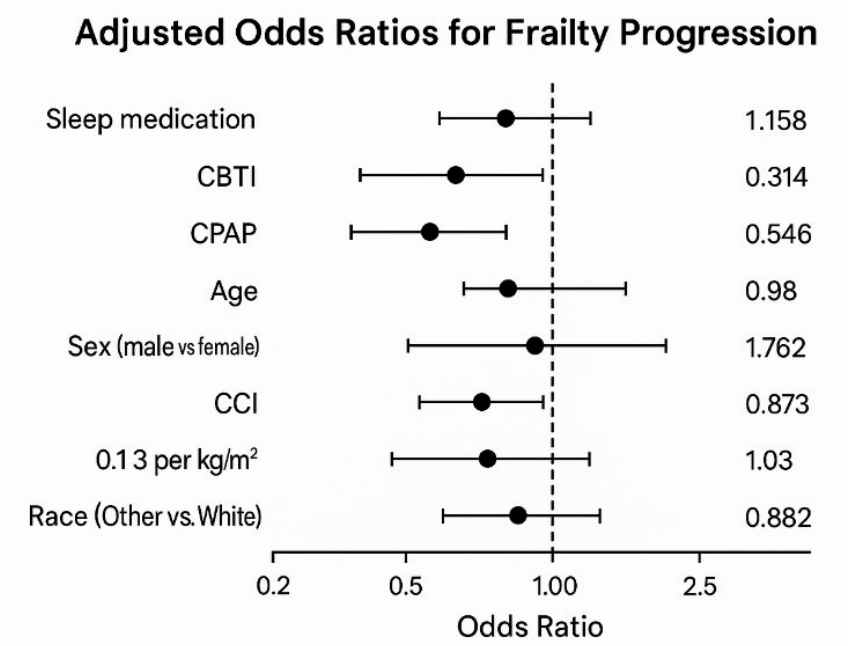
Distributions of Demographic, Clinical, and Frailty Variables



Note. Histograms included overlaid density curves for Age, CCI, and BMI; mean ± SD, while the Bar Graph shows percentage distributions of age group, PTSD status, CCI category, sex, race, ethnicity, ESS, and BMI for the full sample (N = 6824).

Figure 2

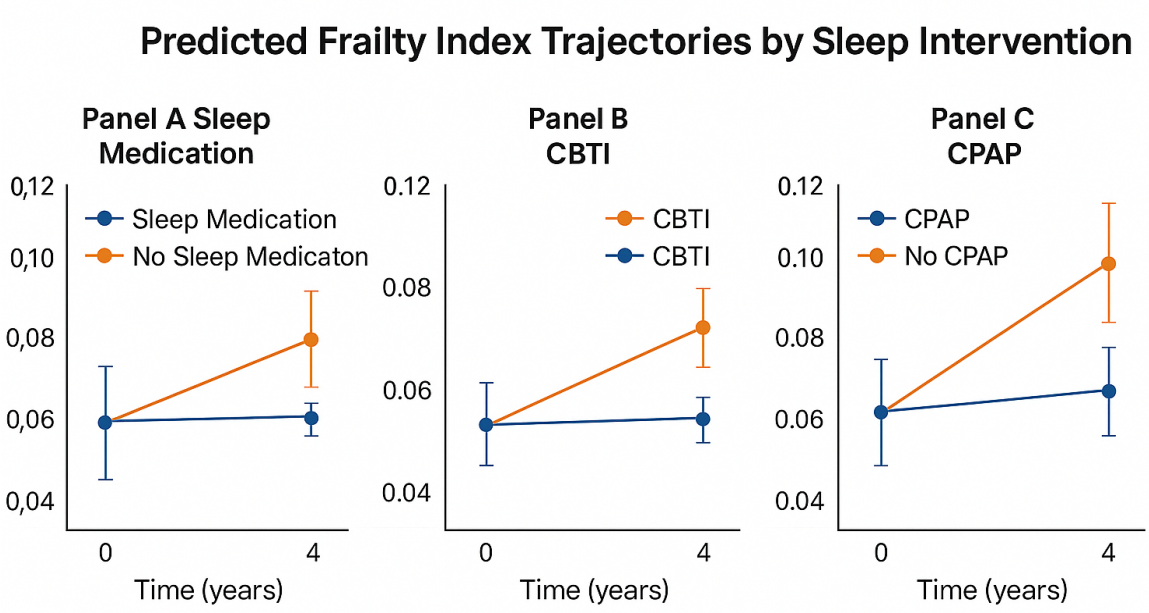
Forest Plot of Logistic Regression Results (Frailty Progression)



Note. Forest plot of adjusted odds ratios (aORs; 95% CIs) for frailty worsening (FI_worth=1) over ~4 years in veterans ≥50 with insomnia (N=6,824). Dashed line at OR=1 indicates null. Models adjust for age, sex, CCI, BMI, and race. aOR<1 = lower odds; aOR>1 = higher odds.

Figure 3

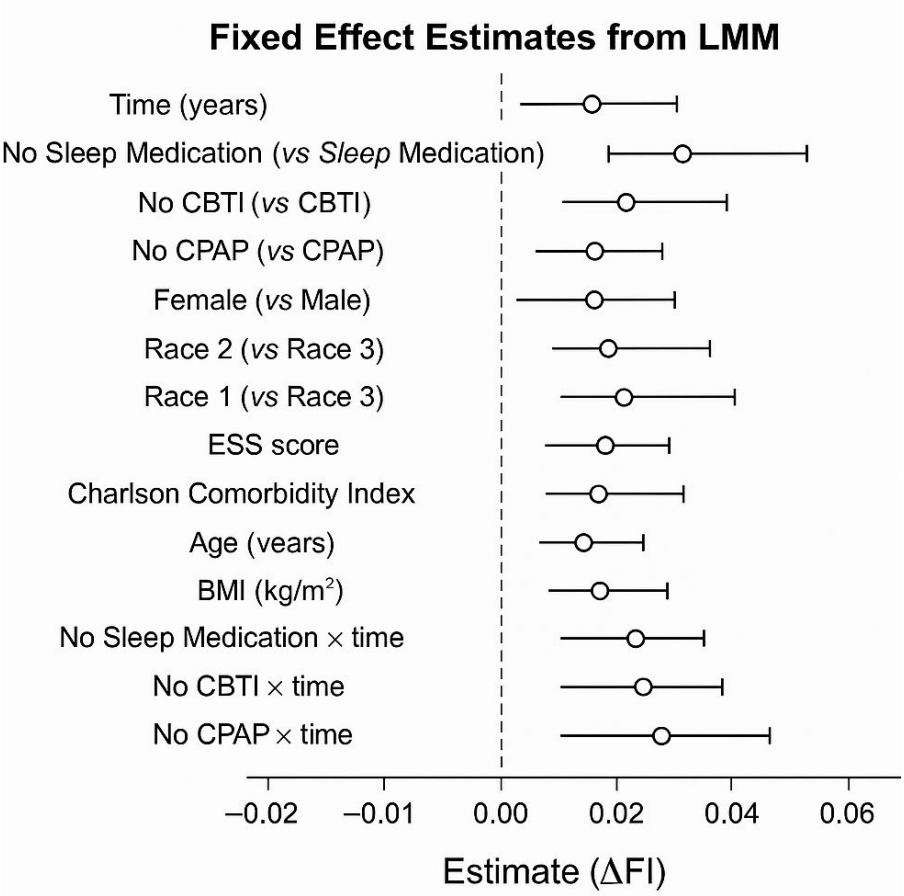
Predicted FI Trajectories by Sleep Intervention From B/L to F/U



Note. Predicted marginal means of the FI at baseline (0 years) and 4-year follow-up, adjusted for age, sex, BMI, and CCI. Panel A shows sleep-medication effects, Panel B shows CBT-I effects, and Panel C shows CPAP effects. Error bars represent 95% CI.

Figure 4

Fixed Effect Estimates From Linear Mix Models of FI Changes



Note. Values represent fixed effect estimates (ΔFI) from the linear mixed-effects model with 95% confidence intervals. Positive values indicate increases in the frailty index over time. Predictors include intervention status (Rx, CBT-I, CPAP), time, demographic covariates (age, sex, race), and clinical variables (ESS score, BMI, CCI). Interaction terms capture differential effects of interventions over time.

Discussion

In a national cohort of U.S. veterans aged ≥50 years with insomnia and abnormal ESS, CBT-I and CPAP were associated with more favorable frailty outcomes, whereas

prescription sleep medication was associated with a modest increase in frailty risk. Specifically, CBT-I and CPAP were associated with lower odds of frailty worsening and more favorable FI trajectories over ~4 years, while medication exposure was related to higher FI without evidence of a time-varying benefit. These findings extend prior work showing short-term improvements in sleep continuity, cognition, and mood with CBT-I and CPAP (El Basiouny & Habib, 2023; Aboussouan et al., 2023) by demonstrating associations with a broader, longer-term health marker—frailty. They align with emerging evidence that enhancing sleep continuity and nocturnal oxygenation may buffer physiologic decline and functional impairment (Wang et al., 2024; Xue et al., 2024). In a population prone to multimorbidity, sleep disruption, and functional vulnerability (Bourassa et al., 2024), these results support the Clinical Epidemiology focus on real-world effectiveness: interventions that modify sleep behavior or physiology may reduce exposure to stressors (inflammation, cognitive decline, impaired performance) that contribute to deficit accumulation (Wen et al., 2023; Xu et al., 2024). The absence of a medication×time effect suggests that, despite symptomatic relief, pharmacologic therapy may not meaningfully alter frailty trajectories and may carry longer-term functional tradeoffs, consistent with concerns about sedative-hypnotics in older adults (Simon et al., 2024).

Limitations

Several limitations warrant consideration. First, the observational design precludes causal inference; despite adjustment for age, sex, BMI, CCI, and race, residual confounding, particularly confounding by indication and adherence, may persist (e.g.,

individuals receiving CBT-I or CPAP may differ in motivation, access, or baseline health) (Kim et al., 2022). Second, although I used a validated Frailty Index, its derivation from administrative data may not capture phenotypic components of frailty (e.g., exhaustion, grip strength), introducing measurement limitations (Piovezan et al., 2023). Third, exposures were coded as binary indicators (any sleep medication, any CBT-I, any CPAP) without information on dose, duration, or adherence (e.g., CPAP hours/night; CBT-I session count; medication class and dosage), which can attenuate or distort associations. Fourth, I did not model time-varying exposure or apply survival/immortal-time methods, because intervention status was summarized over the observation window, temporal ordering between exposure and change in frailty cannot be assured, and time-related bias cannot be excluded. Fifth, potential confounders not included in the models—such as PTSD or depression severity, OSA severity, sedative class/polypharmacy, pain, physical activity, and socioeconomic factors—may influence both treatment selection and frailty trajectories. Sixth, the binary worsening endpoint (FI_worsen) entails information loss relative to continuous FI and may yield different inferences; I therefore emphasize convergent findings across both outcome scales. Seventh, model performance for the logistic specification explained a modest proportion of variance (Nagelkerke $R^2 \approx 0.04$), and results should be interpreted as population-level associations rather than individual risk predictions. Eighth, the cohort was predominantly male veterans, which may limit generalizability to nonveteran and female populations (DeBellis et al., 2023). Finally, ESS values were extracted using NLP from clinical notes; misclassification is possible despite validation (Walker et al., 2020).

Implications

For veterans aged ≥50 years with insomnia and abnormal ESS, these findings support prioritizing CBT-I and CPAP as first-line strategies and exercising caution with long-term prescription sleep medications, which were associated with greater frailty burden over time. In routine care, incorporating ESS screening and FI tracking can help identify patients at elevated risk and monitor response to therapy, while pathways that default to CBT-I (in-person or digital) and prompt evaluation for OSA with CPAP initiation when indicated may mitigate frailty progression (El Basiouny & Habib, 2023; Aboussouan et al., 2023; Xue et al., 2024; Wang et al., 2024). Within integrated systems such as the VHA, low uptake of nonpharmacologic interventions observed in this cohort argues for expanded access (e.g., tele-CBT-I), adherence support for CPAP, and medication stewardship with time-limited courses and deprescribing reviews when feasible (DeBellis et al., 2023; Simon et al., 2024). Conceptually, the results reinforce frailty as a modifiable outcome responsive to upstream sleep interventions that may reduce inflammatory and functional stressors contributing to deficit accumulation (Pourmotabbed et al., 2020; Wen et al., 2023; Xu et al., 2024; Piovezan et al., 2023).

For research, future evaluations should quantify treatment intensity and adherence (e.g., CBT-I session dose; CPAP hours/night; medication class/dose), incorporate time-varying exposure or prospective designs to clarify temporality, and report absolute effects alongside adjusted odds ratios to guide clinical decision-making. Priority work in underrepresented subgroups (e.g., women veterans, advanced age strata, baseline frailty categories) and mechanistic studies testing whether improvements in sleep continuity and

nocturnal oxygenation mediate changes in FI would refine targeting and inform guideline development (El Basiouny & Habib, 2023; Aboussouan et al., 2023; Wang et al., 2024; Xue et al., 2024).

Recommendations

Future work should prioritize randomized controlled trials to test the causal effects of CBT-I and CPAP on frailty progression, with long-term follow-up and standardized frailty assessments to complement the observational evidence presented here (Xue et al., 2024; Wang et al., 2024). In parallel, prospective and high-quality observational studies should capture treatment adherence and dosage (e.g., CBT-I session counts, CPAP hours/night, medication class and dosage) and integrate patient-reported outcomes to clarify mechanisms linking improved sleep continuity and nocturnal oxygenation to reductions in frailty burden. Prespecified subgroup analyses—particularly by PTSD status, other mental health comorbidities, and race/ethnicity—are needed to evaluate effect modification and address health disparities in this population (Bourassa et al., 2024; Byrne et al., 2021). Finally, implementation studies in real-world geriatric and veteran settings should identify and remediate barriers to CBT-I and CPAP uptake and adherence (e.g., access, training, telehealth delivery, device support), thereby informing scalable pathways for deployment where the need is greatest (Aboussouan et al., 2023).

Conclusion

In a national cohort of veterans aged ≥50 years with insomnia and abnormal ESS, CBT-I and CPAP were associated with lower odds of frailty worsening and more favorable FI trajectories over ~4 years, whereas prescription sleep medication was

associated with greater frailty burden. Although observational, these findings link sleep-focused care to a broader geriatric outcome and support prioritizing nonpharmacologic and OSA-targeted strategies with ongoing functional monitoring in routine practice. Confirmation in randomized or pragmatic trials that incorporate treatment intensity and adherence is needed, but implementation of scalable CBT-I and CPAP programs within veteran care may help reduce frailty-related morbidity and promote healthier aging.

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Does Frailty Progression Differ Between Veterans with sEDS and Insomnia with or Without PTSD?

Mona Amirmazaheri

Department of Public Health, Walden University

Supported by the Department of Veteran Affairs, Michael E. De Bakey VA Medical Center (MEDVAMC), Baylor College of Medicine (BCM)

All findings and conclusions are solely those of the authors.

Outlet for Manuscript

Journal of Traumatic Stress (JTS) is an ideal venue for the manuscript, *"Does Frailty Progression Differ Between Veterans with sEDS and Insomnia with or Without PTSD?"* The study sits squarely within JTS's scope by examining if PTSD, a core journal focus, modifies the relationship between sleep disruption (sEDS, in the context of insomnia) and long-term physical health trajectories (frailty). Leveraging a large, nationally representative VHA cohort with ~4 years of follow-up, validated Frailty Index endpoints, and multivariable longitudinal modeling, the work advances trauma science beyond symptomatology to quantify aging-related morbidity linked to PTSD and co-occurring sleep disturbance. This integration of psychology, psychiatry, epidemiology, and public health aligns with JTS's interdisciplinary mission and its interest in mechanisms (stress physiology), heterogeneity of effects (PTSD×time interaction), and clinical translation (trauma-informed geriatric care). The manuscript can be formatted as a full empirical article with a structured abstract (Background, Method, Results, Conclusions), APA style references, and clearly labeled tables/figures reporting effect sizes, 95% CIs, and exact *p* values. Standard psychological and epidemiologic terminology is used throughout; methods emphasize reproducibility (cohort definition, FI construction, covariate adjustment, model diagnostics). Ethically, the study describes IRB/R&D approvals and data provenance from the VHA CDW. For JTS readers, clinicians, researchers, and policy stakeholders, the paper offers: (a) novel evidence that PTSD modestly accelerates frailty progression in veterans with insomnia and sEDS; (b) quantification of sEDS as a stable risk marker for elevated frailty level; and (c)

implications for trauma-informed, integrated care pathways (screening for sEDS/PTSD, prioritizing evidence-based sleep interventions). The manuscript therefore meets JTS's criteria of clarity, rigor, and relevance to traumatic stress and its multidimensional health impacts, with direct implications for practice and policy in high-risk veteran populations.

Keywords: Subjective Excessive Daytime Sleepiness (sEDS), Insomnia, PTSD, Frailty Index, Veterans, Longitudinal Cohort

Highlights

- In veterans ≥50 with insomnia and sEDS, PTSD modestly accelerates frailty over ~4 years (PTSD×time significant).
- sEDS marks a higher frailty level independent of age, BMI, CCI, sex (no ESS×time effect).
- Large VHA cohort (N=6,824) with LMM and adjusted logistic models strengthens inference.
- Findings support trauma-informed, integrated sleep–geriatric care to mitigate frailty.

Abstract

Frailty, a multidimensional syndrome of diminished physiological reserve, is common in older veterans. Subjective excessive daytime sleepiness (sEDS) and insomnia are prevalent and linked to functional decline, while posttraumatic stress disorder (PTSD) is associated with stress-system dysregulation and accelerated aging. In this study it was tested whether PTSD modifies frailty trajectories in veterans aged ≥50 with insomnia and sEDS. Using Veterans Health Administration corporate data warehouse records, a retrospective cohort was assembled with documented ESS scores and an insomnia diagnosis (N = 6,824); sEDS was defined as ESS≥11, and PTSD was identified via ICD-9/10 codes. Frailty was measured with the FI at baseline and ~4-year follow-up. Multivariable (ΔFI) and LMM assessed longitudinal associations among PTSD, sEDS (ESS continuous), and FI, adjusting for age, sex, BMI, CCI, and race; sleep-treatment indicators (CBT-I, CPAP, prescription medication) were explored. Overall, 18.0% experienced worsening of frailty. Veterans with PTSD had higher ESS (p=.044) but similar baseline FI. In regression, PTSD showed a small inverse association with ΔFI (β=−0.017, p=.020), whereas in LMM the PTSD×time interaction was significant (B=0.001, p=.008), indicating a modestly steeper FI trajectory with PTSD. Higher ESS, BMI, CCI, and male sex were associated with higher FI; age inversely related to change. Sleep-treatment indicators correlated with higher follow-up FI, consistent with confounding by indication. In veterans with insomnia and sEDS, PTSD was associated with modest acceleration of frailty over 4 years, supporting stress-process accounts of trauma's physiological burden and underscoring the need for trauma-informed, integrated

care; future studies should test biologic mediators and whether earlier PTSD and sleep interventions attenuate frailty risk.

Introduction

Problem Focus

Frailty progression in aging veterans represents a significant concern for public health, particularly in the presence of comorbid conditions such as sEDS and PTSD. Veterans aged 50 and older represent a population with distinct healthcare needs, characterized by an increased prevalence of sleep disorders and mental health conditions. SEDS, defined as persistent daytime sleepiness despite adequate nocturnal rest, has been associated with adverse health outcomes, including frailty. PTSD, a condition highly prevalent in this population, is linked to chronic stress dysregulation and accelerated biological aging, factors that may contribute to frailty progression. Despite the clinical significance of these conditions, limited research has examined the interaction between sEDS and PTSD and their combined impact on frailty progression, representing a critical gap in the literature. In this study, the association between PTSD and frailty progression among veterans with insomnia and sEDS, evaluating whether PTSD modifies the relationship between sEDS and frailty, has been estimated. By estimating the combined effects of sEDS and PTSD on frailty progression, this analysis provides empirical evidence to support the development of targeted clinical strategies for frailty prevention and management. The findings have the potential to inform healthcare interventions aimed at reducing frailty-related morbidity and improving health outcomes in aging veterans.

Significance/Importance

Assessing the combined impact of sEDS and PTSD on frailty progression is essential due to the clinical and public health implications associated with frailty in aging populations. Frailty is a multidimensional syndrome characterized by decreased physiological reserves, increased susceptibility to stressors, and increased risk of adverse outcomes such as falls, hospitalization, and mortality. Estimating the association between sEDS, PTSD, and frailty progression enables the identification of high-risk individuals, and the assessment of targeted interventions designed to mitigate frailty-related complications**.** Veterans experience an elevated risk of adverse health outcomes due to service-related exposures, with the interaction between mental health conditions and physical decline contributing to reduced quality of life and increased healthcare utilization. This study examines the association between sleep disorders, PTSD, and frailty progression, addressing the intersection of sleep medicine, gerontology, and mental health. The findings may provide epidemiologic evidence to support targeted clinical interventions aimed at improving health care outcomes in aging veterans. This study examines the association between sEDS and PTSD with frailty progression, assessing the mechanisms through which these conditions contribute to physical decline. Identifying these associations is critical for informing targeted interventions aimed at reducing frailty-related morbidity and improving long-term health outcomes in aging veterans.

Theoretical Framework

The Stress Process Model (SPM) provides the theoretical framework for this study, offering a structured approach to evaluating the impact of sEDS and PTSD on frailty progression. SPM conceptualizes stress as an outcome of the interaction between stressors, coping resources, and individual resilience, which collectively influence the health trajectory. Within this framework, the study assesses both the direct associations between sEDS, PTSD, and frailty, as well as the potential modifying effects of coping resources and mental health interventions on frailty progression.

Relevant Scholarship

Existing research has established a strong association between sleep disorders, PTSD, and adverse health outcomes, particularly in aging veteran populations. Sleep disorders, including insomnia, sleep-disordered breathing, and sEDS, are highly prevalent among veterans and have been linked to cognitive impairment, mood disorders, reduced quality of life, and increased risks of falls, fractures, and even mortality (Byrne, S. P. et al., 2021). SEDS, characterized by impaired sleep-wake regulation and an increased tendency for unintended sleep episodes despite sufficient nocturnal rest, is a recognized risk factor for adverse health outcomes in older adults (Wu, W. et al., 2024). Veterans, who exhibit a higher prevalence of comorbid conditions, experience sEDS at disproportionately high rates, further increasing their susceptibility to physical decline and frailty (Shrauner, W., Lord, E. M., Nguyen, X. M. T., 2022; Hernández-Ruiz, V. A., Erlandson, K. M., Amieva, H., & Avila-Funes, J. A., 2022).

Frailty, a multidimensional geriatric syndrome characterized by diminished physiological reserve and heightened susceptibility to adverse outcomes, including falls, hospitalization, and mortality, serves as a significant predictor of long-term health trajectories in aging populations (Soysal, P. et al., 2021; Hou, C. et al., 2020). Studies have shown that frailty is not only prevalent among older adults but also has been reported in younger veterans, particularly those with chronic conditions such as sleep disturbances (Kim, W. J. et al., 2022; Alqahtani, B. A., 2021; Shrauner, W. et al., 2022). The cumulative exposure to physical and psychological stressors during military service is associated with an increased risk of both frailty and sleep disorders like sEDS in veterans (Prguda, E., & Dwyer, M., 2024). Evidence indicates that sEDS is associated with an increased risk of frailty progression through mechanisms involving accelerated physical decline, impairing mobility, and a higher prevalence of chronic conditions such as cardiovascular disease and diabetes (Sánchez-De-La-Torre, M. et al., 2023; Shrauner, W. et al., 2022; Hou, C. et al., 2020). Sleep disorders have also been linked to impaired physiological recovery from daily physical and cognitive stressors, further contributing to frailty progression (Keil, S. A. et al., 2023). PTSD, a condition with high prevalence among veterans, has been extensively studied for its associations with both mental and physical health (Nagy, S. M. et al., 2022). PTSD is characterized by intrusive thoughts, hyperarousal, avoidance behaviors, and negative alterations in mood and cognition (Swift, K. M., 2020). The chronic stress associated with PTSD has been linked to adverse physical health outcomes, including hypertension, cardiovascular disease, diabetes, and ultimately, frailty (Swift, K. M., 2020). PTSD contributes to physiological dysregulation

through sustained activation of the hypothalamic-pituitary-adrenal (HPA) axis and inflammatory pathways, which may accelerate physical decline and predispose individuals to early-onset frailty (Giroux, C., & Sciolla, A. F., 2024; Leistner, C., & Menke, A., 2020). Evidence indicated that PTSD is associated with biological dysregulation and an aging acceleration process, characterized by cumulative physiological wear-and-tear, a phenomenon referred to as "accelerated aging" (Palgi, Y., 2020). This process is particularly relevant in assessing frailty risk among veterans with comorbid PTSD and sleep disorders, as it may contribute to early functional decline and increased susceptibility to adverse health outcomes (Bourassa, K. J. et al., 2024).

While the independent effects of sEDS and PTSD on health outcomes have been extensively studied, their combined influence on frailty progression remains insufficiently examined (Pruiksma, K. E., Taylor, D. J., Wachen, J. S., Straud, C. L., ... & 2023). Existing research primarily examines sEDS and PTSD as independent risk factors, with limited studies assessing their potential synergistic effects on frailty progression. Given the high prevalence of both conditions among veterans, this population provides a critical context for investigating their combined impact (Prguda, E., & Dwyer, M., 2024). Veterans experience a higher burden of comorbidities and stress-related health conditions compared to the general population, making them a well-defined cohort for examining the combined effects of sEDS and PTSD on frailty progression (Zimmer, Z., Korinek, K., Young, Y., Teerawichitchainan, B., & Toan, T. K., 2022). Emerging evidence indicates that co-occurring PTSD and sleep disorders such as sEDS may have a compounding effect on health outcomes. Studies have demonstrated that individuals with PTSD exhibit

a higher prevalence and severity of sleep disturbances, which can exacerbate PTSD symptoms, contributing to a cyclical pattern of health deterioration (Taylor, D. J., Pruiksma, K. E., Mintz, J., ..., 2023). This bidirectional association between PTSD and sleep disorders, particularly sEDS, has been implicated in progressive cognitive and physical decline over time. Studies indicate that veterans with PTSD exhibit an increased risk of developing chronic conditions such as obesity, diabetes, and cardiovascular disease, all of which are established risk factors for frailty (Messman, B. A., Fentem, A., Compton, S. E., Griffith, E. L., Blumenthal, H., Contractor, A. A., & Slavish, D. C., 2023). Veterans with PTSD experience higher levels of inflammation, oxidative stress, and neuroendocrine dysregulation, physiological mechanisms that have been linked to increased frailty risk (Pivac, N., Vuic, B., Sagud, M., ... & Mimica, N., 2023; Muhie, S., Gautam, A., Yang, R., ... & Jett, M., 2023; Lawrence, S., & Scofield, R. H., 2024). Despite increasing recognition of the health consequences associated with sEDS and PTSD, limited research has examined their combined impact on frailty progression in veterans. Existing studies primarily assess these conditions independently, underscoring the need for investigations into their interactive effects on long-term health outcomes. Given the high prevalence of both sEDS and PTSD in veterans, evaluating their potential synergistic influence on frailty progression is essential for understanding whether their co-occurrence exacerbates health deterioration beyond the effects of either condition alone. The potential interaction between PTSD and (sEDS) may accelerate frailty progression in aging veterans. Although the independent associations of PTSD and sEDS with adverse health outcomes are well-documented, their combined impact on frailty

remains insufficiently studied. Given the high prevalence of both conditions in veterans, evaluating their joint effects is essential for identifying potential synergistic influences on frailty risk. Investigating this relationship may support the development of targeted interventions that integrate mental and physical health strategies to improve frailty management in this high-risk population (Hernández-Ruiz et al., 2022; Bourassa et al., 2024).

Research Questions and Design

The primary research question in this study is: What is the longitudinal association between sEDS and frailty progression in veterans aged 50 and older with insomnia, after controlling for age, sex, BMI, and Charlson Comorbidity Index (CCI)?

The study examines whether PTSD modifies the association between sEDS and frailty progression in this population. This research question addresses a critical gap in literature, as existing studies have primarily examined the independent effects of sEDS and PTSD on physical and mental health outcomes. However, the potential interaction between these conditions and their combined influence on frailty progression remains insufficiently investigated. In this study, I aim to evaluate whether PTSD modifies the association between sEDS and frailty progression. Identifying this potential interaction is essential for developing targeted interventions that address both mental and physical health concerns in aging veterans. A retrospective cohort design is employed to examine the longitudinal impact of sEDS and PTSD frailty, accounting for prior exposure to these conditions and their influence on health trajectories over time. The longitudinal analytical approach to examine associations between sEDS, PTSD, and frailty progression using

repeated measures data from a large veteran cohort has been used in this study. The utilization of electronic medical records (EMRs) from the Veterans Health Administration (VHA) enables a robust statistical analysis of these relationships, accounting for potential confounders and improving the precision of effect estimates. Enhancing the validity of the findings, the analysis incorporates adjustments for confounding variables, including age, BMI, race, ethnicity, sex, and CCI, which have been established as determinants of health outcomes. Statistical modeling accounts for these factors to estimate the independent associations of PTSD and sEDS with frailty progression. This research is framed within the theoretical context of the SPM, which provides a framework for understanding how stressors, such as PTSD and sEDS, impact health outcomes like frailty. The SPM is applied in this study to examine the association between chronic stressors, including PTSD and sEDS, and frailty progression. This model is used to assess whether PTSD and sEDS function as independent or interacting factors contributing to frailty risk. The analysis incorporates EMR-derived variables, including demographic characteristics, clinical indicators, sleep-related assessments, and mental health diagnoses, to quantify these relationships within a veteran population. The primary outcome is the changes in the Frailty Index over time, stratified by PTSD and sEDS status. The analysis compares frailty progression between veterans with PTSD and sEDS and those without PTSD, adjusting for demographic and clinical covariates. This approach quantifies the interaction between mental and physical health conditions in aging veterans and supports the development of evidence-based strategies for frailty management in this high-risk population.

Methods

Study Approval and Data Source

This retrospective cohort study was approved by the Institutional Review Board (IRB) of Walden University, Baylor College of Medicine (BCM), and the Research and Development (R&D) Committee of the Michael E. DeBakey VA Medical Center (MEDVAMC). The study utilized EMRs from the VHA Corporate Data Warehouse (CDW), a nationally integrated relational database that consolidates patient data from all VHA healthcare facilities across the United States. The CDW contains comprehensive records of inpatient and outpatient encounters from 2019 to 2023, including diagnostic codes, prescribed medications, laboratory results, vital signs, and physician notes. This data set facilitates analysis across all three manuscripts, examining associations between insomnia, sEDS, frailty progression, and related treatment interventions among veterans. Participants aged ≥50 were included in this study to align with the aging veteran population. The CDW data set is structured for longitudinal analyses, enabling a comprehensive assessment of sleep disorders, frailty, and their interrelationships while adjusting for demographic, clinical, and psychological variables. The data set incorporates sleep-related service encounters and interventions classified under ICD-9/10 and CPT systems, facilitating an in-depth examination of health outcomes in this veteran population. Baseline and follow-up data points were analyzed to assess frailty progression over time, supporting a detailed assessment of the longitudinal associations between sleep disorders, PTSD, and frailty.

Cohort Selection

The study population consists of veterans aged 50 years and older, selected due to the higher prevalence of sleep disorders and frailty in this age group. Veterans with a diagnosis of posttraumatic stress disorder (PTSD) were specifically included based on evidence indicating an increased susceptibility to sleep disturbances and frailty, likely influenced by the cumulative effects of military-related physical and psychological stressors. This cohort provides a relevant study population for examining the associations between insomnia, sEDS, PTSD, and frailty progression within an aging veteran demographic. The final analytic sample consisted of 6,824 veterans with documented ESS scores in their medical records. Within this cohort, 3,859 participants were classified in the Normal-ESS group (ESS $\leq$10), while 2,965 participants were categorized in the High-ESS group (ESS $\geq$11). The priori power analysis was performed to determine the sample size required to detect statistically significant differences in frailty progression between veterans with and without PTSD, stratified by ESS scores. The analysis was based on α level of 0.05 and a desired power of $1 - \beta = 0.80$, adhering to established epidemiologic research standards. The substantial sample size derived from the VHA database provides adequate statistical power to assess the associations between sEDS, PTSD, and frailty progression with epidemiologic precision and reliability.

Variables and Data Sources

The primary exposure variable for this study is sEDS, assessed using the ESS, a validated instrument for measuring daytime sleepiness severity. Participants were stratified into two groups based on ESS scores: Normal-ESS (ESS 0–10) and High-ESS

(ESS 11–24). This classification is used to examine differential associations between varying levels of daytime sleepiness and frailty progression. PTSD status was assessed as a mediating variable using diagnostic documentation from the VHA, identified through International Classification of Diseases (ICD) codes. PTSD was categorized as a binary variable (0 = No, 1 = Yes) to evaluate its potential effect modification on the association between sEDS and frailty progression. Evaluating PTSD as a potential effect modifier in frailty progression is essential, given its established association with sleep disturbances and adverse health outcomes. This assessment provides insight into the interaction between mental and physical health in this population. Frailty progression serves as the primary outcome measure, assessed through changes in FI over 4 years. Data were collected at two time points: baseline, defined as the date of insomnia diagnosis, and a follow-up, occurring 4 years later. The longitudinal design facilitated a comprehensive assessment of frailty progression over time. The primary outcome measure, the Frailty Index (FI), is a validated continuous metric ranging from 0 (absence of frailty) to 1 (Severe frailty), quantifying the cumulative burden of health deficits across physical, cognitive, and functional domains. Higher FI scores denote greater frailty and an increased risk of adverse outcomes, including disability, hospitalization, and mortality. For analytical purposes, FI scores were categorized as follows: Robust: $FI \leq 0.10$; Pre-frail: $FI > 0.10$ and $FI \leq 0.20$; Frail: $FI > 0.20$ (Minici, D., 2023).

These categories were consistently applied at both baseline and follow-up to assess changes in frailty status over time. The FI serves as a standardized measure of an individual's health trajectory, providing a comprehensive evaluation of frailty

progression and its associated risks throughout the study period. To further assess frailty progression, the concept of "frailty worth" was utilized, defined as the difference between follow-up FI (FI_final) and baseline FI (FI0). This measure was categorized as follows: No worsening of frailty (FI_final - FI0 ≤ 0), indicating a stable or improved health status (0); Worsened frailty status (FI_final - FI0 > 0), indicating a decline in health (1). This classification facilitated a targeted analysis of frailty progression, particularly identifying participants with worsening frailty status over the study period (Kaskirbayeva et al., 2023). By quantifying these dynamic changes, the study provides valuable insights into the frailty trajectories and the factors influencing frailty outcomes. Control variables included demographic factors (age, sex, race, and ethnicity), as well as BMI and CCI. These covariates were incorporated to adjust for potential confounders and determine that the association between sEDS, PTSD and frailty progression was not attributable to underlying demographic or health-related factors. Additionally, the time interval between the baseline and the final frailty assessment was included to maintain consistency in longitudinal analyses and accurately capture frailty progression over time.

Instrumentation and Measures

The Epworth Sleepiness Scale (ESS) is a validated instrument for assessing subjective daytime sleepiness. It consists of eight self-reported items, with respondents rating their likelihood of dozing off in various situations on a scale from 0 to 3, yielding a total score ranging from 0 to 24. In this study, a score of ≥11 was used to define significant sEDS, facilitating the classification of participants based on sleepiness severity. The Frailty Index **(**FI) is a validated measure used to quantify frailty, based on

the accumulation of health deficits across multiple domains, including physical, cognitive, and functional impairments. The FI is calculated as the ratio of the number of deficits present to the total number of potential deficits considered, providing a continuous measure of frailty status. In this study, the FI was calculated at baseline (defined as the index date of insomnia diagnosis) and at a 4-year follow-up to evaluate frailty progression over time. Health status was assessed using the Charlson Comorbidity Index (CCI), a validated tool for predicting mortality risk based on the presence and severity of comorbid conditions. The CCI, ranging from 1 to 27, quantifies the overall burden of chronic conditions. For analytical purposes, the CCI is categorized into low comorbidity (CCI 0–1) and high comorbidity (CCI ≥2) to facilitate subgroup analyses (Kachlíková et al., 2020). BMI is also included as a health measure and classified as non-obese (BMI < 30) and obese (BMI ≥ 30) (Mohajan & Mohajan, 2023). These variables are incorporated as control factors to adjust for the potential influence of pre-existing health conditions on the association between sEDS, PTSD, and frailty progression, thereby enhancing the validity of the findings. Both the ESS and FI are well-established measures with strong evidence supporting their validity and reliability across diverse populations, particularly in clinical and epidemiologic research. The ESS is widely recognized for its accuracy in assessing daytime sleepiness, while the FI serves as a standard metric for quantifying frailty in older adults. To enhance the internal validity of the study, a Natural Language Processing (NLP) algorithm was implemented to extract ESS scores from unstructured text within the VHA EMRs, ensuring accurate and consistent data retrieval.

Statistical Analysis Strategies

This retrospective cohort study analyzed longitudinal data from the VHA database to examine temporal associations between significant sEDS, PTSD, and frailty progression. The study population included 6,824 veterans, with baseline assessments conducted at year 0 and follow-up at year 4. Adjustment for potential confounders including age, sex, BMI, and the CCI, was performed to strengthen internal validity. This approach reduces the risk of residual confounding, ensuring that the estimated associations between sEDS, PTSD, and frailty progression more accurately reflect true effects rather than confounding bias. The longitudinal design is used to assess frailty progression over time, providing quantitative insights into changes in frailty status in relation to sleep disorders and PTSD. This analytical framework is consistent with the study's objective of examining the impact of stressors, such as sEDS and PTSD, on frailty. The findings provide quantitative evidence with implications for clinical practice and healthcare policy, in addressing stress-related health challenges among aging veterans. Descriptive Analysis**:** Descriptive statistics were performed to summarize the study population, including the distribution of ESS scores, PTSD status, demographic variables (age, sex, race, and ethnicity), and baseline frailty levels measured by the FI. This analysis provided a quantitative overview of cohort characteristics and facilitated the identification of potential confounders for subsequent analyses. Inferential Analysis: To assess the association between PTSD and frailty progression, multivariable logistic regression was conducted, controlling for sEDS, demographic factors (age, sex, race, and ethnicity), BMI, and CCI. Adjusted odds ratios (aOR) with 95% confidence intervals (CI)

were calculated to quantify the strength and direction of the associations. This approach controlled potential confounders, allowing for an isolated assessment of the independent effects of sEDS and PTSD on frailty progression. In addition, linear mixed models (LMM) were considered to analyze the longitudinal impact of PTSD on frailty progression while accounting for the correlated nature of repeated measurements and individual variability. This method accommodates complex interactions and the inclusion of multiple covariates, ensuring a robust assessment of frailty trajectories over time. By integrating both logistic regression and LMM, this analytical framework provides a comprehensive evaluation of the relationship between sEDS, PTSD, and frailty progression. The findings contribute essential evidence to inform veteran healthcare strategies and clinical interventions aimed at mitigating frailty risk in populations with insomnia and sEDS.

Results

The final analytic sample comprised N=6,824 veterans aged ≥50 years with an insomnia diagnosis and documented ESS. Mean (SD) age was 61.79 (7.82) years (range 50–97). Mean (SD) BMI was 31.47 (5.92) kg/m² and mean (SD) CCI was 1.41 (1.83). Mean (SD) ESS was 9.85 (5.91); 43.4% had ESS≥11. Baseline frailty (FI_0) averaged 0.09 (0.09) and increased at ~4-year follow-up (FI_final) to 0.11 (0.10). Frailty worsening (FI_final > FI_0) occurred in 18.0% of participants. Full characteristics are shown in Table 1. Participants were stratified by PTSD status (ICD-9/10). As summarized in Table 2, veterans with PTSD were younger than those without PTSD (61.47 vs 61.99 years), t (5646.20) =2.76, p=.003, d=0.07, and reported higher ESS (10.15 vs 9.68), t (6786)

=2.01, *p*=.044, *d*=0.05. They had slightly lower BMI (31.28 vs 31.58), *t* (5152.54) =2.05, *p*=.020, *d*=0.05. There were no group differences in CCI (*p*=.498), FI_0 (*p*=.130), or FI_final (*p*=.183). Figures 1–2 visualize these distributions. Boxplots (Figure 1) show small separations for age and BMI by PTSD status, with broadly similar distributions for CCI and FI. Violin plots (Figure 2) include ΔFI (FI_final − FI_0) and indicate comparable change distributions across PTSD groups. I estimated a multiple linear regression predicting FI_final from PTSD status, FI_0, age, sex, BMI, CCI, race, and ESS. The model was significant, F (8, 6779) =896.27, p<.001, with adjusted R^2=.513 (Table 3). FI_0 showed the largest association with FI_final (B=0.704, p<.001). PTSD was a small, negative predictor of FI_final (B=−0.017, p=.020). Sex (p=.004), BMI (p<.001), and race (p<.001) were significant covariates; age, CCI, and ESS was not significant. Full coefficients and 95% CIs are provided in Table 3. A second model using ΔFI = FI_final − FI_0 as the outcome with the same predictors yielded a small, explained variance (R^2=.008). PTSD remained a negative predictor of ΔFI (p=.020). Sex (p=.025), BMI (p<.001), and race (p=.006) were significant; age, CCI, and ESS were not. Complete estimates appear in Table 3. I fit an LMM predicting FI at baseline and ~4-year follow-up with time (0, 4 years) as a repeated factor, random intercepts for participants, and fixed effects for PTSD, age, sex, BMI, CCI, and ESS, plus the PTSD×time interaction. All 6,824 participants contributed 13,648 observations. Estimation used REML with an unstructured covariance. Model fit indices indicated adequate fit (AIC=−30,545.03; BIC=−30,514.96). The time effect was significant, F (1, 6786) =380.78, p<.001. The PTSD main effect was not significant, F (1, 6780.16) =1.37, p=.242, and baseline

marginal means did not differ by PTSD status (Δ=0.000; 95% CI −0.004 to 0.004; p=.929). The PTSD×time interaction was significant, F (1, 6786) =6.96, p =.008 (B=0.001; 95% CI 0.000–0.002), indicating a modestly steeper increase in FI over time among veterans with PTSD. Covariates associated with higher FI were ESS (B=0.001, p<.001), CCI (B=0.010, p<.001), and BMI (B=0.001, p<.001); age showed a small inverse association (B=−0.0004, p=.002). The coefficient for sex was B=−0.011 (p=.002). The model converged; parameter estimates were stable. Figure 5 presents fixed-effect estimates (β, 95% CIs), with the largest effects observed for time, CCI, BMI, and ESS; the PTSD×time term is small but significant. Figure 6 shows model-predicted FI at both points by PTSD status; both groups increased over time, with a slightly steeper trajectory for the PTSD group. To describe intervention-related profiles, estimated marginal means at the 2-year point from the same LMM are shown in Figure 8: medication users had higher predicted FI than nonusers (0.095 vs 0.075), CBT-I recipients 0.096 vs 0.075, and CPAP users 0.091 vs 0.081. These contrasts are descriptive and align with the covariate-adjusted model predictions; numerical estimates and CIs appear in Table 4.

Table 1

Descriptive Statistics for the Total Sample

Variable	M	SD	Minimum	Maximum
Age (years)	61.79	7.82	50.0	97.0
BMI (kg/m²)	31.47	5.92	10.49	67.14
CCI (Index)	1.41	1.83	0	15

ESS (Sleepiness)	9.85	5.91	0	24
FI_0 (Baseline)	0.09	0.09	0.00	1.00
FI_final (Follow-up)	0.11	0.10	0.00	1.00

Note. FI_0 = baseline Frailty Index score; FI_final = Frailty Index at 4-year follow-up. All continuous variables are untransformed and reflect observed values without imputation. Scores were calculated using available EMR data from the VHA CDW system, N=6,824

Table 2

Descriptive Statistics Stratified by PTSD Status

Variable	PTSD = No (n = 4,399)	PTSD = Yes (n = 2,389)
Age (years)	61.99 (SD = 8.25)	61.47 (SD = 6.95)
BMI (kg/m^2)	31.58 (SD = 6.04)	31.28 (SD = 5.69)
CCI	1.42 (SD = 1.84)	1.42 (SD = 1.84)
ESS	9.68 (SD = 5.86)	10.15 (SD = 5.96)
FI_0 (Baseline)	0.09 (SD = 0.09)	0.09 (SD = 0.09)
FI_final (Follow-up)	0.11 (SD = 0.10)	0.11 (SD = 0.10)

Note. Values presented as M (SD). PTSD status was classified using the ICD-9/10 code documented in the VA medical record. Differences in age, BMI, and ESS between PTSD groups were statistically significant (see Table 3). No differences were observed in the comorbidity burden or frailty scores

Table 3

PTSD Versus Non-PTSD Groups Comparison

Variable	t	df	p	Cohen's d
Age	2.76	5646.20	.003	0.07

ESS	2.01	6786	.044	0.05
BMI	2.05	5152.54	.020	0.05
FI_0	-1.13	4970.47	.129	-0.03
FI_final	0.90	5069.72	.183	0.02
CCI	0.01	6786	.498	0.00

Note. Welch t-tests used for age and BMI (unequal variances per Levene). Two-tailed p values. Cohen's d (pooled SD); benchmarks: 0.2/0.5/0.8 = small/medium/large. Age, BMI, and ESS were significant, with small effect sizes.

Table 4

Regression Models Predicting Frailty at B/L & 4-Years F/U

Predictor	B	SE	β	t	p	95% CI for B
(Constant)	0.024	0.010	—	2.478	.013	[0.005, 0.043]
PTSD	-0.004	0.002	-0.017	-2.015	.044	[-0.007, 0.000]
Age	0.000	0.000	-0.015	-1.625	.104	[0.000, 0.000]
CCI	0.000	0.000	0.005	0.595	.552	[-0.001, 0.001]
Sex	0.009	0.003	0.025	2.919	.004	[0.003, 0.014]
ESS	0.000	0.000	0.016	1.826	.068	[0.000, 0.001]
BMI	0.001	0.000	0.049	5.659	<.001	[0.001, 0.001]
Race_cat	-0.006	0.001	-0.038	-4.362	<.001	[-0.009, -0.003]
FI_0 (baseline FI)	0.772	0.010	0.704	80.516	<.001	[0.753, 0.791]

Note. FI_final = frailty at 4-year follow-up; FI_0 = baseline. Coding: PTSD (0=no, 1=yes); sex (0=F, 1=M); race dummy-coded (ref=White). Standardized β reported. Model adjusts for FI_0. All VIFs <1.2.

Table 5

Linear Regression Predicting Change in FI (ΔFI = FI_final − FI₀)

Predictor	B	SE	β	t	p	95% CI for B
(Constant)	0.009	0.010	—	0.911	.362	[-0.011, 0.029]
PTSD	-0.004	0.002	-0.028	-2.322	.020	[-0.008, -0.001]
Age	~0.000	0.000	-0.008	-0.604	.546	[0.000, 0.000]
CCI	-0.002	0.000	-0.054	-4.342	<.001	[-0.003, -0.001]
Sex	0.007	0.003	0.028	2.244	.025	[0.001, 0.013]
ESS	0.000	0.000	0.003	0.225	.822	[0.000, 0.000]
BMI	0.001	0.000	0.045	3.641	<.001	[0.000, 0.001]
Race_cat	-0.004	0.001	-0.034	-2.764	.006	[-0.007, -0.001]

Note. ΔFI = follow-up − baseline FI. Coding: PTSD (0=no, 1=yes); sex (0=F, 1=M); race dummy-coded (ref=White). Abbrev.: Standardized β reported. Baseline FI not modeled (outcome is ΔFI). All VIFs <1.2.

Table 6

Fixed Effects Estimates From LMM Predicting FI Over Time

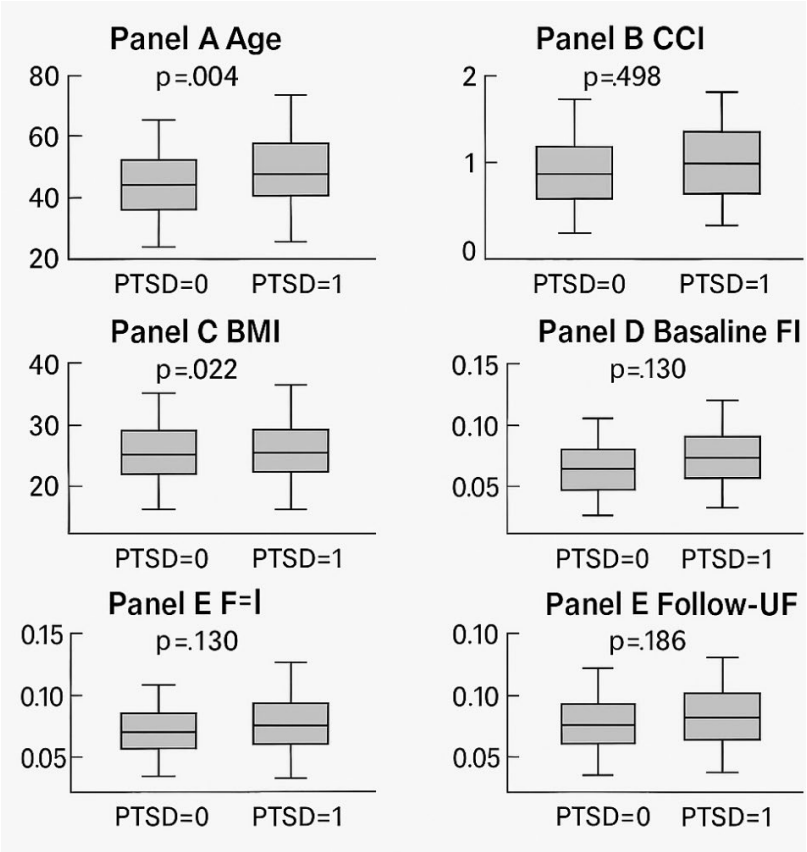
Predictor	B	SE	df	t	p	95% CI for B
Intercept	0.054	0.011	6806.12	4.71	<.001	[0.031, 0.076]
PTSD	-0.003	0.002	6780.16	-1.17	.242	[-0.007, 0.002]
Sex (Male)	-0.011	0.004	6781.00	-3.11	.002	[-0.018, -0.004]
ESS	0.001	0.000	6781.00	5.26	<.001	[0.001, 0.001]
CCI	0.010	0.001	6781.00	17.12	<.001	[0.009, 0.011]
Age	-0.0004	0.000	6781.00	-3.11	.002	[-0.001, 0.000]
BMI	0.001	0.000	6781.00	8.14	<.001	[0.001, 0.002]
Time	0.004	0.000	6786.00	10.48	<.001	[0.003, 0.005]

PTSD × Time	0.001	0.000	6786.00	2.64	.008	[0.000, 0.002]

Note. PTSD (0=no, 1=yes); sex (0=F, 1=M). Time = baseline and follow-up. Covariates (ESS, CCI, age, BMI) are mean-centered. Estimates via REML. Random subject intercepts; unstructured within-subject covariance for time.

Figure 1

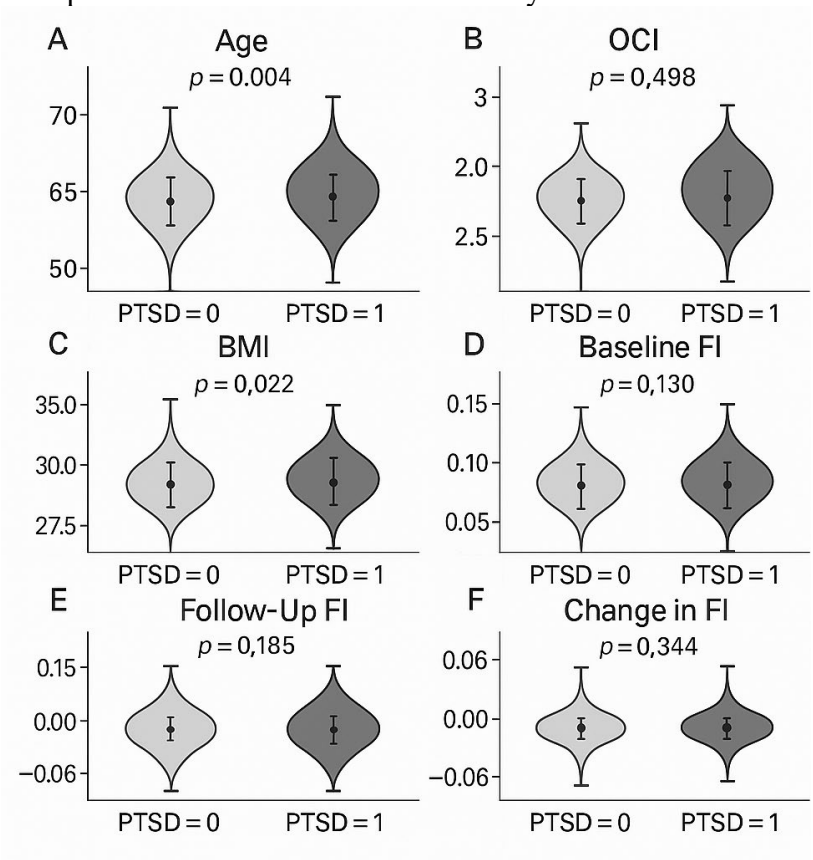
Boxplots Comparing Continuous Variables by PTSD Status



Note. Each panel displays the distribution of a health-related continuous variable for veterans with and without PTSD. Panel A: Age (p = .004); Panel B: CCI, p = .49); Panel C: BMI, p = .02); Panel D: FI_0, p = .130; Panel E: (FI_final, p = .186). Boxes represent the interquartile range (IQR); horizontal lines indicate the median; whiskers extend to 1.5

× IQR. p-values reflect results from two-sided independent samples t-tests. Significant differences were found for age and BMI, though effect sizes were small.

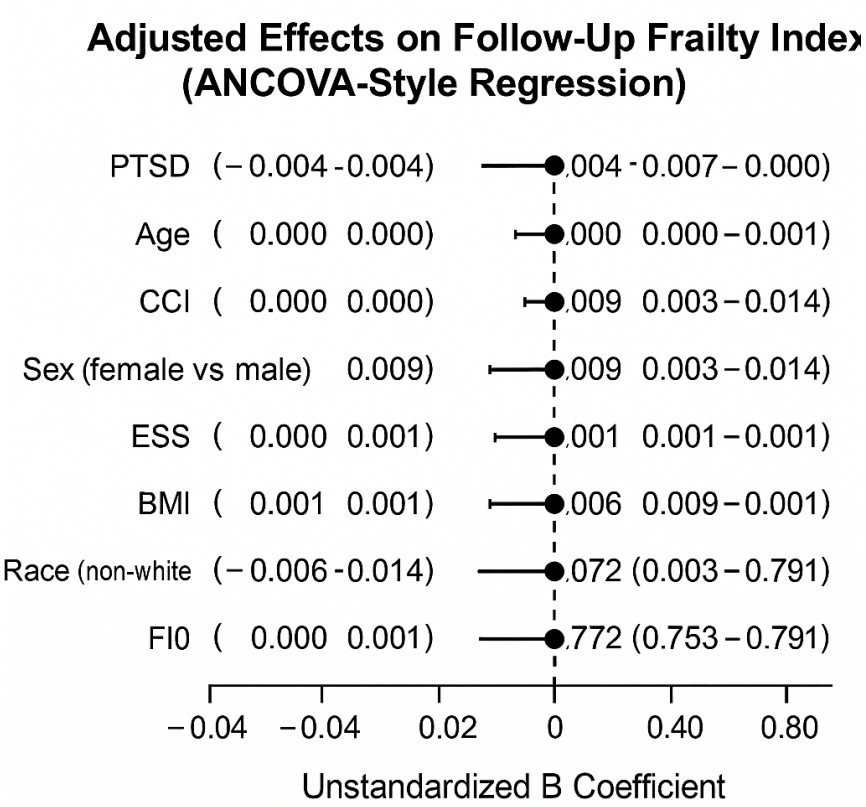
Figure 2
Group Differences in Health Indicators by PTSD Status



Note. Each panel shows the distribution of one continuous variable: Panel A = Age, Panel B = Charlson Comorbidity Index (CCI), Panel C = Body Mass Index (BMI), Panel D = Baseline Frailty Index (FI_0), Panel E = Follow-up Frailty Index (FI_final), and Panel F = Change in Frailty Index ($\Delta FI = FI\_final - FI_0$). Shaded regions indicate kernel density estimates. Central point's denote sample means, and vertical bars represent 95% confidence intervals. Annotated p-values reflect two-sided independent samples t-tests. Significant differences were observed only for age and BMI.

Figure 3

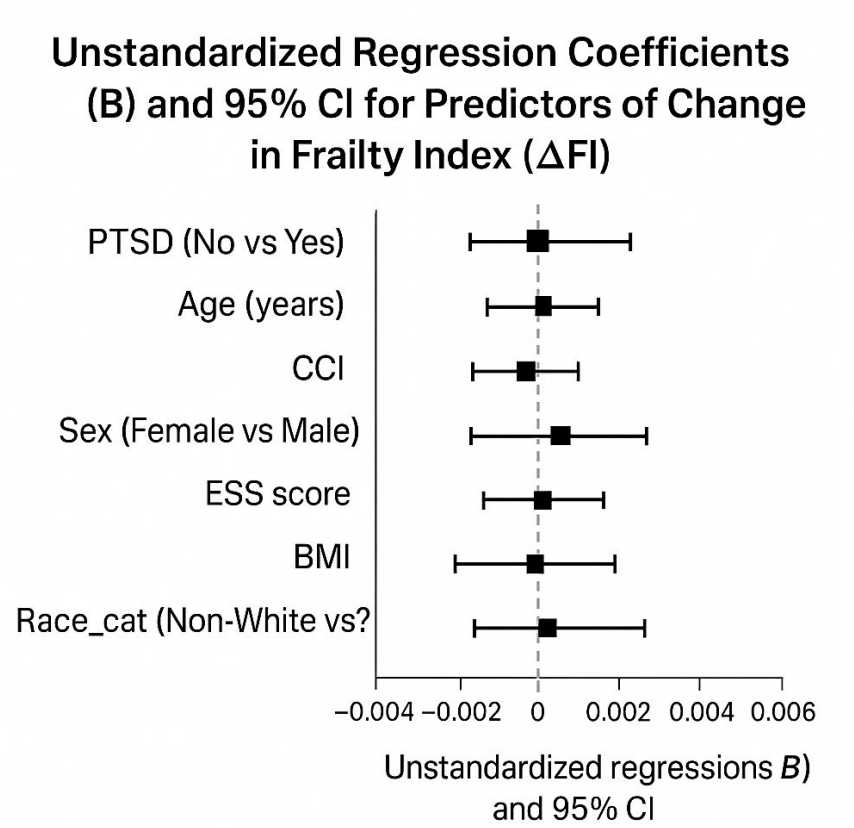
Model Coefficients for Frailty at 4-year Follow-up



Note. The model includes PTSD status, age, sex, BMI, CCI, race category, ESS, and FI_0 as covariates. Values are derived from ANCOVA-style regression. Horizontal bars indicate 95% confidence intervals. Predictors with intervals not crossing zero are statistically significant ($p < .05$). FI_0 is the strongest predictor of follow-up frailty, while PTSD shows a small, inverse association.

Figure 4

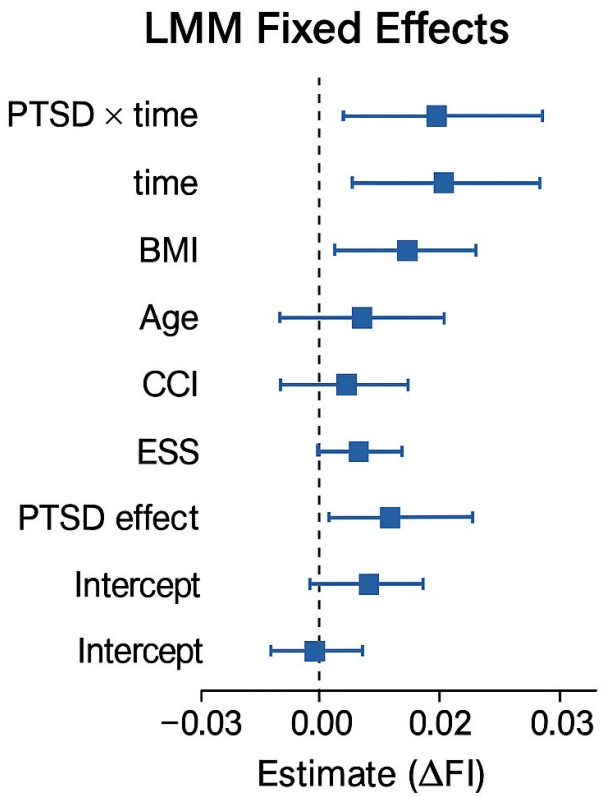
Model Coefficients for Frailty Changes



Note. Predictors include PTSD status, age, sex, BMI, CCI, race category, and ESS score. Squares represent the unstandardized B coefficients from linear regression, and horizontal bars indicate 95% CI. PTSD was associated with a small but statistically significant negative change in frailty (i.e., lower frailty progression), while CCI, BMI, race, and sex were also significant predictors. Confidence intervals crossing zero indicate nonsignificant effects.

Figure 5

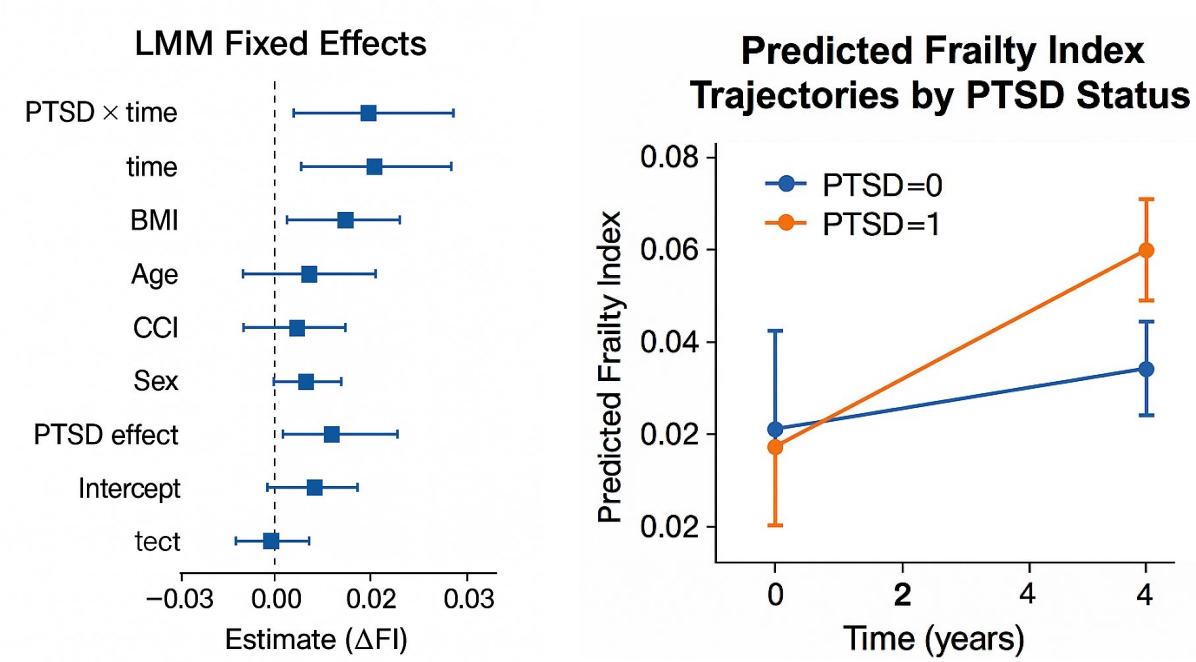
Fixed-Effect Estimates for Frailty Over Time



Note. Estimates are unstandardized coefficients (B) with 95% confidence intervals. Variables include time, PTSD, their interaction (PTSD × time), and covariates: sex, age, BMI, CCI, and ESS. A dashed vertical line at zero indicates the null effect. Time, CCI, ESS, and BMI were significant predictors of increased frailty. PTSD × time was also significant, reflecting a slightly accelerated frailty trajectory among veterans with PTSD. PTSD alone was not a significant predictor.

Figure 6

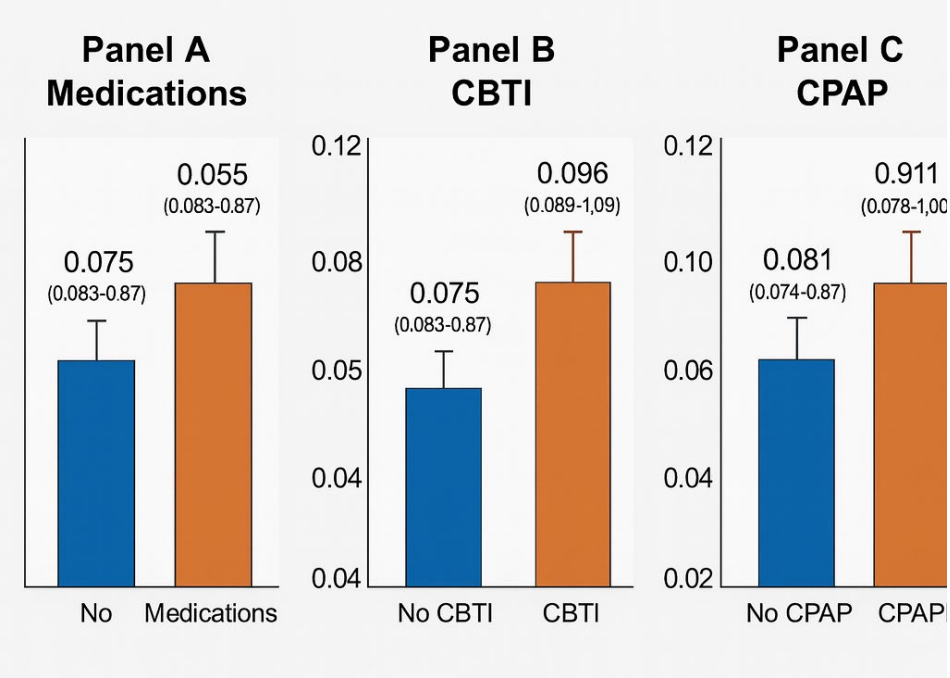
Predicted Frailty Trajectories by PTSD Status Over 4 Years



Note. Lines represent predicted frailty index values from the linear mixed-effects model for veterans with PTSD (orange) and without PTSD (blue). Both groups show progressive increases in frailty over time, but the PTSD group demonstrates a slightly steeper slope, consistent with the significant PTSD × time interaction in the model.

Figure 7

Predicted Frailty at 4-Year Follow-up by Sleep Interventions



Note. Bars represent estimated marginal means of the frailty index at two-year follow-up derived from linear mixed-effects models. Panel A compares participants who did versus did not receive sleep-related medications; Panel B compares recipients and nonrecipients of cognitive behavioral therapy for insomnia (CBT-I); Panel C compares CPAP users to nonusers. Error bars indicate 95% confidence intervals. Predicted frailty scores were slightly higher among participants who received interventions, which may reflect confounding by indication (i.e., those receiving treatment may have had greater baseline impairment)

Discussion

This study provides longitudinal evidence that PTSD is modestly but significantly associated with accelerated frailty progression among older veterans with insomnia and

sEDS. Rather than a higher frailty level at a single time point, the effect appeared as a steeper multiyear slope: the PTSD×time term in the LMM was significant (small magnitude; adjusted for age, sex, BMI, CCI, ESS), whereas the PTSD main effect and baseline group difference in FI were not. This pattern is consistent with stress-process accounts in which chronic psychological stressors impose cumulative physiologic burden that emerges over time (Leistner & Menke, 2020; Lawrence & Scofield, 2024). It also accords with evidence linking trauma to accelerated biological aging (Bourassa et al., 2024) and long-term frailty risk following war exposure (Zimmer et al., 2022). The absence of a baseline FI difference in our cohort may reflect survivor effects, delayed physiologic expression, or heterogeneity in symptom chronicity (Palgi, 2020; Giroux & Sciolla, 2024). Several covariates tracked with higher frailty in adjusted models: higher ESS, higher BMI, and greater comorbidity (CCI) were each associated with higher FI, reinforcing literature connecting daytime sleepiness and insomnia to functional decline (Soysal et al., 2021; Wu et al., 2024; Byrne et al., 2021; Taylor et al., 2023) and the synergy between metabolic/comorbidity burden and deficit accumulation (Mohajan & Mohajan, 2023; Kaskirbayeva et al., 2023). Age showed a small inverse association with change, consistent with survivorship dynamics in aging cohorts. Approximately 18% of participants experienced frailty worsening over ~4 years, indicating clinically relevant progression at the population level. Exploratory, model-based contrasts of sleep-treatment indicators (CBT-I, CPAP, prescription medication) were associated with higher predicted FI at follow-up; given the observational design, these patterns likely reflect confounding by indication (i.e., more symptomatic veterans being more likely to receive

treatment) rather than causal harm and should be interpreted cautiously. Overall, the findings underscore the multifactorial nature of frailty in trauma-exposed older adults and support trauma-informed, integrated care that addresses PTSD, sleep disturbance (including sEDS), and cardiometabolic comorbidity.

Limitations

This observational EMR study cannot establish causality; although PTSD was associated with a steeper increase in frailty, residual confounding (e.g., physical activity, nutrition, socioeconomic context, trauma severity, depression, pain, alcohol use, or OSA severity) may persist. PTSD identification via ICD-9/10 codes is vulnerable to misclassification/underdiagnosis (Muhie et al., 2023). The Frailty Index, while validated, was derived from administrative data and may underrepresent phenotypic and social domains of frailty (Hernández-Ruiz et al., 2022). Measures of sEDS (ESS) and PTSD were treated as baseline indicators; time-varying symptom severity was not modeled, and frailty was available at only two time points, limiting trajectory resolution. Indicators for CBT-I, CPAP, and prescription medication were exploratory, lacked dose/adherence details, and were not analyzed with time-to-treatment methods; thus, observed associations likely reflect confounding by indication rather than causal effects. The cohort, drawn from VHA users, was predominantly older, male, and medically complex, which may limit generalizability to women, nonveterans, and more diverse populations. Finally, although the PTSD×time interaction was statistically significant, the effect size was small; its clinical significance warrants confirmation in studies with richer measurement (e.g., symptom trajectories, adherence) and causal designs.

Implications

Taken together, these findings suggest that PTSD functions as a risk marker for accelerated aging, warranting closer surveillance for early functional decline in veterans with insomnia and sEDS. In clinical workflows, integrating brief PTSD screening with routine sleep (ESS) and frailty (FI) monitoring could enable earlier, trauma-informed intervention before deficits consolidate; this is consistent with stress-process accounts that frame PTSD as a dynamic risk factor whose physiological impact accrues over time (Lawrence & Scofield, 2024). The small but significant PTSD×time effect, alongside the observation that ~18% of patients worsened over ~4 years and that higher ESS, BMI, and CCI tracked with higher FI, argues for integrated geriatric–behavioral health models that address trauma, sleep disturbance, and cardiometabolic comorbidity within veteran-serving systems. Exploratory contrasts of sleep-treatment indicators (CBT-I, CPAP, prescription medication) showed higher predicted FI among treated patients; although these associations likely reflect confounding by indication, they highlight the need to tailor sleep care to frailty risk and to attend to treatment timing, dose, and adherence in trauma-affected populations (Prguda & Dwyer, 2024; Pruiksma et al., 2023). This aligns with critiques of one-size-fits-all insomnia management and supports trauma-informed adaptation of behavioral and device-based therapies (Rigley et al., 2022; Pagel, 2021). At a policy level, embedding trauma-informed screening and stepped sleep care into VHA geriatric pathways, paired with outcome tracking using FI, may reduce downstream medical burden and help preserve independence in vulnerable veterans.

Recommendations

Future work should employ prospective, preregistered designs with structured clinical PTSD interviews (e.g., CAPS-5) and multidomain frailty measurement that integrates deficit-accumulation and phenotypic elements (fatigue, gait/grip, functional limitation, social vulnerability), assessed at multiple time points to capture nonlinearity and time-varying symptom severity. Studies should incorporate biologic mediators—inflammation (e.g., CRP, IL-6), HPA-axis markers (diurnal cortisol), and cellular aging indices (epigenetic clocks)—to clarify mechanisms linking PTSD/sleep disturbance to frailty (Pivac et al., 2023; Bourassa et al., 2024). Intervention research is needed to test whether trauma-focused psychotherapies and multimodal sleep strategies (e.g., CBT-I augmented with OSA evaluation/CPAP adherence programs) can slow frailty progression, building on models from Taylor et al. (2023) and Prguda & Dwyer (2024). To strengthen causal inference, future analyses should measure adherence/dose (CBT-I session counts, CPAP hours/night, medication class/dose) and apply time-varying exposure methods (e.g., MSMs/IPTW) alongside sensitivity analyses (e.g., negative controls, E-values). Subgroup analyses by race/ethnicity, gender, PTSD chronicity, and OSA severity may reveal effect modification (Bourassa et al., 2024). Finally, extending these investigations to nonveteran and international cohorts will enhance generalizability and inform global health-aging strategies (Hou et al., 2020), with results reported using absolute effects (risk differences) and clinically meaningful change thresholds for frailty to guide practice.

Conclusion

In this national cohort of veterans aged ≥50 years with insomnia and sEDS, PTSD was not associated with higher baseline frailty, but it was associated with a modest, statistically significant acceleration in frailty over ~4 years after adjustment for age, sex, BMI, CCI, and ESS. This time-dependent effect aligns with chronic stress and aging models, suggesting that trauma-related burden accrues gradually rather than presenting as a static deficit. Clinically, the findings support trauma-informed, integrated geriatric care, including routine PTSD screening alongside ESS and frailty monitoring, and earlier mental health intervention to potentially blunt downstream physical decline. By linking psychological trauma to longitudinal changes in a broad geriatric health marker, this study deepens understanding of aging in high-risk veterans and highlights opportunities for prevention-oriented, multidisciplinary care.

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Part 3: Summary

This dissertation examines how sEDS, sleep treatments, and PTSD shape frailty trajectories in U.S. veterans aged ≥50 years with insomnia, using linked, longitudinal electronic medical records. Across three interrelated studies (N≈6,800), sEDS, measured by the ESS, consistently marked a higher frailty burden and greater odds of worsening over ~4 years, independent of age, comorbidity, and body mass index. Notably, sEDS elevated the level of frailty but did not accelerate its *rate* of change. In contrast, PTSD did not relate to higher baseline frailty yet showed a significant interaction with time, indicating a modest acceleration of frailty progression. Treatment modality mattered: nonpharmacologic care, for Insomnia CBT-I and, where indicated, CPAP, aligned with lower odds of frailty worsening and more favorable predicted frailty profiles than pharmacologic therapy. Taken together, the findings support a stress-process account of aging in which chronic sleep disturbance confers persistent vulnerability, and trauma exposure adds a time-dependent physiological burden. Practically, the work argues for routine, low-cost screening with the ESS to identify high-risk individuals; prioritization of CBT-I and CPAP within veteran care; and integration of trauma-informed mental health services into geriatric pathways. Methodologically, pairing continuous frailty indices with binary worsening endpoints provided complementary insights while underscoring the importance of avoiding information loss from dichotomization alone. Future research should incorporate time-varying exposures and adherence, test biological mediators (inflammation, HPA-axis, epigenetic aging), and evaluate pragmatic

interventions to quantify absolute risk reductions. Overall, the dissertation advances a data-driven, integrated approach to preventing functional decline in aging veterans

Integrated Findings Across Studies

Study 1 showed that veterans with abnormal ESS (≥11) had persistently higher frailty burden and greater odds of frailty worsening over ~4 years (e.g., aOR≈1.16) without evidence of an ESS×time interaction. Thus, sEDS functioned as a stable risk marker—elevating the level of frailty, rather than accelerating the rate of increase.

Study 2 found that pharmacologic insomnia treatment was associated with higher frailty risk, whereas CBT-I and CPAP were associated with lower odds of frailty worsening and lower predicted FI across time. Where the main effects were small, time-dependent terms suggested more favorable trajectories for CPAP. These patterns underscore the potential long-term advantages of nonpharmacologic and OSA-targeted approaches for sleep health.

Study 3 demonstrated that PTSD was not associated with higher baseline frailty, but the PTSD×time term in linear mixed models was significantly positive, indicating a modest acceleration of frailty over ~4 years among veterans with sEDS and insomnia.

Across all three studies, frailty progression tracked with comorbidity burden (CCI), elevated BMI, and subjective sleep disturbance, reflecting the multifactorial nature of frailty (Soysal et al., 2021; Keil et al., 2023). The identification of sEDS as a distinct, measurable predictor adds to the literature that often emphasizes nocturnal sleep parameters alone.

Alignment With Theoretical Framework

Findings align closely with the Stress Process Model (SPM): chronic stressors, physiological (sleep disruption, sEDS) and psychological (PTSD), contribute cumulatively to dysregulation and functional decline. The absence of an sEDS×time effect (Study 1) alongside the presence of a PTSD×time effect (Study 3) suggests that sEDS marks a persistently higher vulnerability level, whereas PTSD adds time-dependent burden, consistent with SPM's conceptualization of primary vs. compounding stressors. In parallel, the Clinical Epidemiology Framework (Study 2) helped quantify real-world intervention associations: the protective profiles of CBT-I and CPAP bolster the case for nonpharmacologic, evidence-based sleep care in geriatric practice.

Unanticipated Findings

PTSD's lack of association with baseline frailty, despite strong ties to chronic illness, likely reflects survivorship, delayed physiological expression, or heterogeneity in symptom chronicity. Yet the PTSD×time interaction indicates faster frailty accrual over time among those with PTSD, highlighting the insidious, cumulative nature of trauma-related stress. In some adjusted models, age showed a small inverse association with change—again consistent with survivorship/specification effects rather than a truly protective effect of age. Finally, exploratory LMM contrasts in Study 3 showed higher predicted FI among treated patients (CBT-I/CPAP/Rx), which most plausibly reflects confounding by indication and does not contradict Study 2's adjusted protective associations for CBT-I/CPAP.

Implications for Positive Social Change

Routine, low-cost ESS screening can support early risk stratification for frailty in veterans with insomnia. Health systems should expand access to CBT-I (including tele-

delivery) and OSA evaluation with CPAP, while practicing medication stewardship in older adults (time-limited courses, deprescribing reviews). Given PTSD's time-dependent association with frailty, trauma-informed screening and referral should be embedded within geriatric pathways. Collectively, these steps can inform clinical guidelines, VHA policy, and public health strategies aimed at reducing frailty-related disability and resource burden in aging veterans.

Future research directions include:

- Conduct prospective studies (preregistered) using structured clinical PTSD interviews (e.g., CAPS-5) and multidomain frailty measures (deficit accumulation + phenotypic components such as fatigue, gait/grip, social vulnerability) assessed at multiple time points.
- Model time-varying exposures and adherence/dose (CBT-I session counts; CPAP hours/night; medication class/dose) using methods that mitigate time-related bias (e.g., IPTW/MSMs), and report absolute effects (risk differences, NNT) alongside relative measures.
- Test biologic mediators (inflammation, HPA-axis function, epigenetic clocks) to clarify mechanisms linking trauma/sleep disruption to frailty (Pivac et al., 2023; Bourassa et al., 2024).
- Run intervention trials evaluating trauma-focused psychotherapies and multimodal sleep strategies (CBT-I + OSA management) in veterans with comorbid PTSD and insomnia; build on Taylor et al. (2023) and Prguda & Dwyer (2024).

- Perform subgroup analyses (race/ethnicity, sex, service era, PTSD chronicity, OSA severity) and extend to nonveteran/international cohorts to enhance generalizability (Hou et al., 2020).

Lessons learned include:

- Large-scale EMR analyses are feasible and informative but require rigorous preprocessing of unstructured data (e.g., NLP extraction for ESS).
- Integrating clinical, psychological, and demographic variables—and collaboration across sleep medicine, psychiatry, gerontology, and epidemiology—improves inference and translational relevance.
- Using both continuous FI and binary worsening yielded complementary insights; however, dichotomization sacrifices information and should be paired with continuous-scale modeling.

Conclusion

Across three studies in a national cohort of veterans aged ≥50 with insomnia, sEDS was associated with a persistently higher frailty burden and greater odds of worsening, while PTSD was associated with a modest acceleration in frailty over time. CBT-I and CPAP aligned with more favorable frailty profiles than pharmacotherapy, supporting behavioral and OSA-targeted strategies within veteran care. Collectively, these results underscore the biopsychosocial complexity of frailty and the importance of addressing sleep health and mental health together to prevent age-related decline in high-risk populations. The ESS emerges as an accessible, low-cost tool for early identification of veterans at elevated risk for frailty.

Final takeaways are the following:

- sEDS is a clinically useful risk marker for higher frailty burden and worsening; CBT-I/CPAP shows more favorable profiles than pharmacologic treatments.
- PTSD modestly accelerates frailty progression, particularly when co-occurring with sleep disturbance.
- Frailty reflects accumulated psychosocial stressors and sleep-related dysregulation, not chronology alone.
- Integrated, trauma-informed, sleep-focused care is urgently needed in VHA and geriatric health systems.

Together, these findings support routine ESS-based risk stratification, prioritization of CBT-I/CPAP, and trauma-informed geriatric pathways in the VHA to reduce frailty-related morbidity and improve quality of life in aging veterans.

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