EPIDEMIOLOGY AND MECHANISMS OF ADVERSE HEARING OUTCOMES IN US MILITARY SERVICE MEMBERS AND VETERANS OF RECENT WARS

By

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CERTIFICATE OF APPROVAL

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ABSTRACT OF THE DISSERTATION
Epidemiology and Mechanisms of Adverse Hearing Outcomes in US Military Service Members and Veterans of Recent Wars

By

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Doctor of Philosophy in Epidemiology
Oregon Health & Science University, Portland 2020
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Hazardous noise and blasts are prevalent military occupational exposures that can result in adverse hearing outcomes among US military Service members and Veterans and have profound consequences on health and wellbeing. Significant knowledge gaps exist in understanding the burden of hearing loss and the associations between military exposures and hearing both during and after service. Moreover, little is known about the causal mechanisms that can explain these effects. Evidence that helps fill these gaps will aid the Departments of Defense (DoD) and Veterans Affairs (VA) in designing effective interventions and rehabilitation programs. The overall goal of this dissertation was to estimate: 1) the prevalence of hearing loss by severity; 2) rates of hearing changes during military service as a consequence of occupational noise exposure; and 3) mechanisms of the effect of blast exposure on self-reported hearing difficulty. These aims were designed to rigorously yield practically useful information with the goal of improving hearing health and guiding policy.

This dissertation consists of three related manuscripts. In the first, we estimate the prevalence of hearing loss by severity among Veterans who recently separated from the military and use VA health care. Not all Veterans had a hearing test so, for those without

a hearing test, we predicted their hearing thresholds using Bayesian logic in a multilevel model. Data collected for a separate research study informed our prediction model. Results suggest approximately 9.6% of recently separated Veterans who use VA for the health care have mild hearing loss and prevalence declines exponentially with increasing severity of loss. The second manuscript leverages administrative health care records from a hearing conservation program in the DoD to estimate the average annual rate of hearing change during military service and examined how occupational noise exposure ranking alters that trajectory. To accomplish this aim, the administrative data were linked to data describing military occupation service periods provided by participants in a separate research study and noise exposure rankings from a job exposure matrix. Generally, we observed greater hearing decline in the higher frequencies and with moderate and high noise exposure rankings. The greatest average rate of change observed was 1.1 dB/year at 6000 Hz for a high noise exposure rank. We also observed service branch differences that may be reflective of varying cultures and commitments to hearing conservation. The third manuscript describes a formal causal mediation analysis to examine the direct and indirect pathways linking blast exposure to self-reported hearing difficulty among Service members and Veterans with audiometrically normal hearing. Results of this aim suggest that a positive screen for post-traumatic stress disorder mediates about 41% of the observed association between blast exposures and self-reported hearing difficulties.

This work, which described and quantified hearing loss and the relationship between military exposures and hearing outcomes, provides much needed evidence in the field of hearing science. Combined it provides evidence regarding the potential benefit of reducing military workplace noise exposures and psychological distress that are likely contributing to a high prevalence of hearing loss and hearing complaints among post-9/11 Service members and Veterans.

Dedication

For my husband, Kevin, and sons Nathan and Andrew.

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List of Abbreviations

ANSI	American National Standards Institute
CDE	Controlled Direct Effect
CDW	Corporate Data Warehouse
CI	Confidence Interval
dB HL	Decibels Hearing Level
dB SPL	Decibels Sound Pressure Level
DoD	Department of Defense
DOEHRS-HC	Defense Occupational and Environmental Health Readiness System – Hearing Conservation
HCE	Hearing Center of Excellence
HCP	Hearing Conservation Program
HHIA	Hearing Handicap Inventory for Adults
HLM	Hierarchical Linear Model
Hz	Hertz
IOM	Institute of Medicine
JEM	Job Exposure Matrix
kHz	Kilohertz
MCMC	Markov Chain Monte Carlo
MOS	Military Occupational Specialty
MRP	Multilevel Regression and Poststratification
NCRAR	National Center for Rehabilitative Auditory Research
NDE	Natural Direct Effects
NIE	Natural Indirect Effects
NOISE Study	Noise Outcomes in Servicemembers Epidemiology Study
OR	Odds Ratio
PIE	Pure Indirect Effects
PPR	Prevalence Proportion Ratio
PTA	Pure Tone Average
PTSD	Post-Traumatic Stress Disorder
SD	Standard Deviation
STS	Significant Threshold Shift
TBI	Traumatic Brain Injury
VA	Veterans Affairs
VADIR	VA/DoD Identity Repository

Chapter 1. Introduction & Research Aims

Hearing loss can impact a Service member's fitness for duty, and can result in decreases in health, quality of life, and wellbeing over their lifetimes.[1-4] Prevention of adverse hearing outcomes is a priority for the Departments of Defense (DoD) and Veterans Affairs (VA). Hearing loss is the second most common service-connected disability among all Veterans, second to tinnitus, another auditory injury.[5] For fiscal year 2019, the VA reported there were over 1.3 million Veterans with a hearing loss service-connected disability.[5] That same year, the VA spent $302 million on hearing aids, batteries, and repairs.[6]

Noise exposure is ubiquitous in the military and is a significant contributor to hearing loss.[7,8] However, in 2006 an Institute of Medicine (IOM; now known as The Health and Medicine Division of the National Academies) report highlighted the existence of large knowledge gaps in our understanding about the associations between military noise exposure and hearing among Service members and Veterans.[9] The IOM report noted most hearing outcome data were derived from clinical investigations and lacked generalizability. The reported concluded with a call for more epidemiologic research exploring military noise exposure and hearing.

While noise exposure remains the primary known source of hearing loss, blast exposures also play an important role.[10-12] Many post-9/11 Service members are returning home having been injured by one or more blasts, with the ear being the organ most vulnerable to damage.[13] Hence, blast exposure is increasingly being recognized as a prevalent source of hearing injury. Even in the absence of documented hearing loss, Veterans with a history of blast exposure have reported hearing difficulties in noise and in other complex acoustic environments.[14-16] The mechanisms of these reported hearing deficits in the context of intact hearing are poorly understood and may include non-auditory pathways. Innovative epidemiologic approaches are needed to gain a deeper understanding of adverse hearing outcomes resulting from blast exposure and to develop explanatory theories of these outcomes.

This work is a direct response to the IOM's call for research on hearing outcomes in Service members and Veterans. These efforts focus on Veterans of post-9/11 wars because they are demographically and militarily different, including unique deployment experiences, from Veterans of earlier eras.[17,18] Shifting the focus to recently returned Veterans spotlights opportunities for intervention in younger Veterans for whom the adverse effects of hearing loss might be averted.

The overall objective of this dissertation was to provide empirical data on the burden and mechanisms of adverse hearing outcomes among post-9/11 Service members and Veterans. The aims of this work were to estimate: 1) the prevalence of hearing loss by severity; 2) rates of hearing changes during military service as a consequence of occupational noise exposure; and 3) mechanisms of the effect of blast exposure on self-reported hearing difficulty. The dissertation consists of three manuscripts, organized as follows:

The dissertation begins with a review of literature in Chapter 2, touching on auditory injury as it relates to noise and blast exposures and the current gaps in the literature.

In Chapter 3 (Aim 1), we estimated the prevalence of mild, moderate, and severe hearing loss among Veterans who have recently separated from the military and use VA health care. Prevalence of hearing loss by severity requires measurement of hearing thresholds among Veterans. However, because not all Veterans were evaluated by audiology, such data were not readily available via administrative health care databases. To address this aim, we developed a Bayesian multilevel regression model with poststratification based on audiometric data from Veterans using VA health care and audiometric data from Veterans enrolled in the Noise Outcomes In Servicemembers Epidemiology Study ("NOISE Study"), a prospective study investigating military exposures and auditory outcomes.

In Chapter 4 (Aim 2), we estimated the average change in Service members' hearing over the course of military service and evaluated the effects of noise on changes in hearing over time. This was accomplished by linking audiometric data, collected from military personnel as part of a DoD hearing conservation program, to data describing demographic and military-service characteristics obtained from individuals enrolled in the NOISE Study. The analytic cohort included Veterans who enlisted in military service after September 2001. We examined the longitudinal association between military occupations categorized as having a low, moderate, or high noise exposure ranking and pure-tone hearing thresholds (500-6000 Hz), stratified by service branch, using a hierarchical linear model.

In Chapter 5 (Aim 3), we estimated the effects of blast exposure on self-reported hearing difficulty, and the mediating effects of post-traumatic stress disorder (PTSD) on this relationship. Using regression models and following a formal causal mediation framework, we estimated total associations between blast exposure and hearing difficulty, natural direct and indirect associations, and percent of the observed association mediated through PTSD. Moreover, we used four-way decomposition to disentangle the association between blast exposure and hearing difficulty by PTSD, explaining 'how' and 'for whom' blast exposure tends to affect self-reported hearing ability. Again, this chapter focuses on post-9/11 Service members and Veterans.

In Chapter 6, we conclude by presenting a critical summary of the dissertation's rationale and importance, key study findings, strengths and limitations of the work, as well as public health implications and areas for future research.

Finally, the Appendices provide documentation from the joint VA Portland Health Care System and Oregon Health & Science University Institutional Review Board for Aim 1 and for the NOISE Study, as well as supplemental methods and results for each of the three studies.

Chapter 2. Review of the Literature

2.1. Hearing loss impact on Service members and Veterans

Hearing loss is an unfortunate consequence of war and is an important concern for the US Department of Defense (DoD) and the US Department of Veterans Affairs (VA). Hearing loss limits one's ability to hear high frequency sounds, understand speech, and communicate. For active duty Service members, this can compromise situational awareness, making it difficult to safely perform job tasks.[1,2,19] Thus, hearing loss can impact active duty Service members' fitness for duty. Service members with hearing loss also leave military service at a higher rate than those with normal hearing.[20] Keeping attrition low is important to ensuring a strong military force.

The impacts of hearing loss extend beyond limiting work activities related to military service. In the non-military workplace, individuals with hearing loss report feeling embarrassed and incompetent, and fear for their future employability.[21] Furthermore, individuals with hearing loss have lower employment rates and when employed have lower wages than the general population.[22-24] Hearing loss is also associated with psychosocial health problems including depression, social isolation, anxiety, poor self-esteem, and physical health problems such as increased falls, unintentional injuries, decreased cognitive function, fatigue, decline in functional capacity to conduct tasks of everyday living, and hospitalizations.[3,25-37] Specifically among Veterans, hearing loss has been found to be associated with negative social and emotional outcomes, decreased cognitive function, and depression.[27,38,39] Hence, hearing loss acquired during military service can lead to a lifetime of consequences.

2.2. Noise and blasts associated with adverse hearing outcomes

Noise exposure [>80 decibels sound pressure level (dB SPL)] is the primary cause of hearing loss among Service members.[7,8] It has been said that all Service members will be exposed to hazardous levels of noise at some point during their military career.[8] Not surprisingly then, hearing loss and tinnitus (another auditory injury) are the two most prevalent service connected disabilities in the VA.[5] Noise exposure can cause damage to structures of the inner ear (Figure 2.1). Initially, noise exposure damages the synaptic connections between the inner hair cells and the auditory nerve fibers responsible for carrying auditory sensory information from the cochlea to the cortex.[40-43] Further physiologic damage occurs to the outer hair cells of the cochlea responsible for amplifying low-level sounds.[44] A permanent hearing loss ensues once 30-50% of the ~16,000 outer hair cells are irreparably damaged.[45] Noise exposures typically affect the mid-to-high frequencies of hearing [≥3000 Hertz (Hz)]. Exposure to an intense (>150 dB SPL) impulse noise has the potential to induce an acoustic trauma including eardrum perforation, fractures to the middle ear bones, and rupture of the organ of Corti off the basilar membrane.[46-50] Impulsive noise exposures can result in an immediate, permanent hearing loss affecting a wide range of frequencies.[10,49] The most common complaint among individuals with documented hearing loss is increased difficulty understanding speech in background noise.

Figure 2.1. Illustration of the anatomy of the ear.

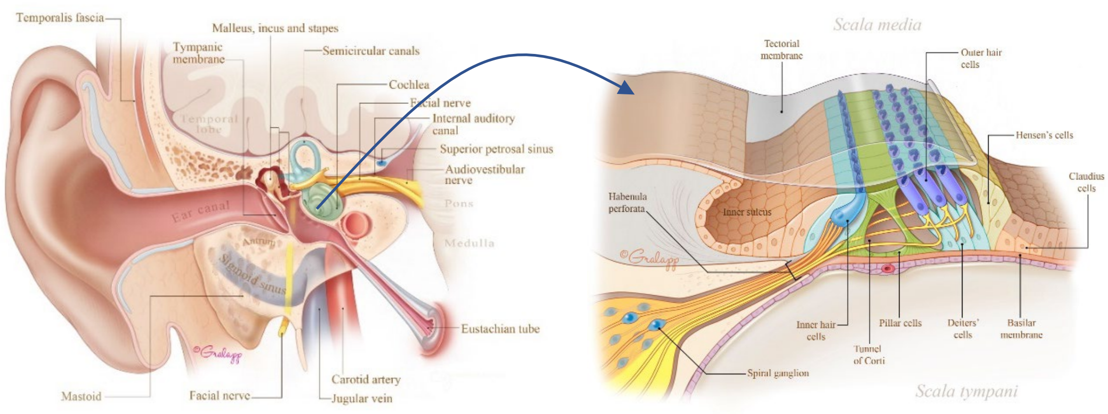

Figure legend: Left – Depiction of the peripheral auditory system. Right – Enlarged cross-section of the cochlea showing the organ of Corti and its inner and outer hair cells responsible for the sound transduction. Reprinted with permission. [Illustration] ©2015 Christine Gralapp, MA, CMI

Blast exposure is also a risk factor for hearing loss.[10,11,14,46] A blast exposure is the sudden release of energy that forms a pressure wave. This pressure wave propagates outward and is followed by a blast wind.[51] Pressure waves can have debilitating effects on the body. The blast wind that follows the pressure wave can propel debris into an individual and/or knock them into a solid object.[51] The ear is particularly vulnerable to the pressure wave because it is the body's most sensitive pressure transducer.[12,13] The initial pressure wave, depending on the distance from the blast, can be accompanied by a high-intensity impulse noise. Both the pressure wave and accompanying high-intensity noise can induce varying degrees of acoustic trauma (described above), irrevocably damaging the peripheral auditory system.[11,29,48,52,53] Insurgence warfare has led to an increase in blast exposures among Service members compared to past (pre-9/11) wars.[51] Between 2005 and 2009, the one-year incidence of any blast injury per 1,000 deployed

Service members ranged from 1.7 to 4.5 but reached levels of 83 per 1,000 deployed among a combat team during a troop surge.[54] The total number of Service members exposed to a blast is difficult to conceive because most estimates are derived from injury databases and not all blasts lead to injury warranting medical care.[51] However, blast exposure is responsible for a substantial portion of Service members killed in action and those who incurred a TBI, 75%[55] and 36%[56] respectively. Since 2001, 5,449 Service members have been killed in action[57] and another 417,503 experienced a TBI.[58] Therefore, we estimate 154,388 Service members have been killed or injured by blast. Today's Service members are more likely than those of past wars to survive blast exposures due to improved personal protective equipment and emergency medical care in the war zone.[51,59] This progress means that more Service members return home with lifelong injuries.

Eardrum perforation is the most common primary blast injury occurring in 17% of blast injured Service members[12] and is usually accompanied by hearing loss in the cochlea.[60] In a sample of deployed male Service members, Joseph and colleagues reported that individuals with a blast-related injury were twice as likely to have hearing loss compared to individuals with a non-blast related injury (OR=2.2; 95% CI: 1.4-3.4).[11] And, while 21% of the individuals had documentable hearing loss based on a hearing test following the blast injury, 45% experienced at least a 15 dB hearing change at one or more frequencies. Forty-nine percent of the risk for hearing loss in deployed male Service members was attributed to the blast event.[11] Less well understood are the effects of blast exposure on the central auditory system (brainstem and higher).[16,61,62] It has been hypothesized that blast exposure can affect the central auditory system in a separate and distinct manner, likely through traumatic brain injury (TBI). There is evidence that shows blast exposure is associated with self-reported hearing difficulty among Veterans with and without hearing loss.[14,16,29,63] Concerning are the Veterans with a history of blast exposure, including blast-induced TBI, and normal hearing sensitivity but who complain of hearing difficulty in the presence of background noise.[14,15,63] This discordant finding has turned hearing scientists' attention toward the potential for sub-clinical damage in the peripheral auditory system, namely the cochlea,[40-42] and increased awareness of the vulnerability of the central auditory system.[16,61] However, the ability to understand speech in noise also requires sustained attention and focus on the target signal, cognitive tasks that mostly remain outside auditory pathways, an area of research that has received relatively little focus.

2.3. Institute of Medicine report highlights gaps in knowledge

With increasing concerns about the impact noise has on our military Service members, Congress directed the VA to contract with the IOM to review the literature from World War II to the present on noise and military service and its impact on the auditory system. In 2006, the IOM report highlighted the existence of large knowledge gaps in our foundational understanding about the epidemiologic associations between military noise exposure and hearing among Service members and Veterans.[64] In a comprehensive review of the literature, the IOM reported most hearing loss data were derived from non-epidemiologic investigations (e.g., small sample sizes, convenience samples, recruited from specialty clinics) that prohibited interpretations of prevalence and incidence of hearing loss among Service members. And, hearing loss outcomes were generally reported as averages, lacked frequency specific thresholds, and reported using definitions that may not be sensitive to early noise-induced hearing changes. Exacerbating these methodological limitations is the hearing science field's lack of prospectively collected data. Generally, proportions of individuals with hearing loss or hearing threshold changes are reported rather than the rate or magnitude of the hearing change.[64] Occasionally, these measures are repeatedly collected and compared over time;[65-67] while repeat cross-sectional evaluations can tell us about the change in the proportion of Service members with hearing loss or significant threshold shifts, it does not capture individual level changes nor allow us to assess how those changes may be a consequence of military exposures.

Since the release of the IOM report, hearing scientists and hearing health care practitioners and administrators have been working to better understand the effects of noise and other military exposures on hearing. The DoD is building infrastructure and processes aimed at supporting this work, including the development of the DoD Hearing Center of Excellence (HCE)[68] and expansion of military policies to audiometrically monitor a greater number of Service members.[69] The military expanded the at-risk hearing conservation program, the Defense Occupational and Environmental Health Readiness System – Hearing Conservation (DOEHRS-HC),[70] to more of a population health program requiring all operational forces to have annual hearing tests coupled with hearing protection and hearing education.[69] Despite the initial enthusiasm, epidemiologic research efforts have been slow. Fourteen years following the IOM report, we still lack valid estimates of the post-service separation prevalence of hearing loss, the rate of hearing change during service, and how noise may alter that trajectory. Acquiring this fundamental knowledge about exposures and hearing outcomes could help inform military service-related interventions, rehabilitation programs, and disability compensation.

2.4. Post-9/11 Veterans: A population of interest

Following the attacks of September 11, 2001, the US launched the Global War on Terrorism, which continues today. Approximately 4.8 million Service members have served since then, of which 3.2 million served only during the post-9/11 era. VA projects a post-9/11 Veteran population of just over 6.2 million by 2030.[17] This is the youngest and most diverse cohort of Veterans served by the VA—nearly half are under the age of 35, about 17% are women, and over one-third are racial or ethnic minorities.[18,71,72] Given the operational demands of post-9/11 conflicts, Service members have been deployed multiple times and deployments have required the mobilization of Service members from reserve components (Reserves and National Guard) much more so than in decades past.[73] Finally, compared to all other service era Veterans, post-9/11 Veterans are more likely to have a service-connected disability and use VA health care only.[71] Thus, the VA has identified these Veterans as a population of interest for ongoing surveillance and investigation of military exposures on health outcomes. The epidemiologic investigation of hearing outcomes is necessary for timely diagnosis, treatment, and rehabilitation in younger Veterans for whom the consequences of hearing loss might be prevented.

2.5. Prevalence of hearing loss among post-9/11 Veterans

Despite hearing conservation efforts, military Service members remain at risk for developing service-related hearing loss requiring post-service diagnosis, rehabilitation, and potential disability compensation. Results of a national survey found that 4% of post-9/11 Veterans self-reported serious difficulty hearing.[74] Military Veterans serving before 9/11 were 1.3 times (adjusted prevalence ratio 95% confidence interval (CI): 1.2-1.4) more likely than non-Veterans to report serious difficulty hearing, while Veterans serving between 9/11 and March 2010 were four times (adjusted prevalence ratio 95% CI: 2.7-6.0) more likely.[74] This observed association underscores the need for continued investigation into the risk factors for hearing loss, especially among post-9/11 Veterans. While surveys allow for the collection of data that might otherwise be prohibitively expensive to undertake, they are limiting in that subjective reports do not always agree with objectively collected measures. One study compared self-report incident hearing loss in military Service members to an objective hearing test and found moderate agreement between the two measures, which suggests there is some misclassification that will impact underlying estimates of prevalence when hearing loss is defined by self-report.[75]

Little is known about the prevalence of hearing loss among the population of post-9/11 Veterans using audiometric criteria.[76] Hearing loss is typically diagnosed based on the results of an in-depth audiometric assessment. Audiometry is the process of measuring hearing ability using pure tone stimuli, which measures the smallest detectable levels (threshold) of pure tones at varying frequencies, typically 250 to 8000 Hz. One approach to estimating the prevalence of hearing loss is to extract disability claims from administrative databases, which presumably relies on the audiometric assessment. Recently, the VA reported that, among post-9/11 Veterans, hearing loss was the 10th most prevalent service-connected disability, affecting 2.1% of this population.[77] However, the VA definition of hearing disability (>40 dB HL at a single frequency from 250 to 4000 Hz) is likely to miss mild hearing losses and hearing losses in the higher frequencies (6000 and 8000 Hz). Subsequently, disability claims can be expected to underestimate the prevalence of hearing loss among Veterans. Mild hearing loss and high frequency hearing loss can impose difficulties in everyday life and should not be underestimated.

Another approach to estimate the prevalence of hearing loss is to extract diagnostic codes for hearing loss from health care databases that reflect a diagnosis based on audiologic assessments. To date, only two population-based studies have investigated the prevalence of hearing loss among post-9/11 Veterans and both used diagnostic codes; Frayne et al[78] and Swan et al[79] reported the prevalence of hearing loss diagnosis as 19% and 13%, respectively, and noted that males had a higher prevalence of hearing loss compared to females. While informative, the use of diagnostic codes to estimate prevalence is limiting. First, diagnostic codes used for epidemiologic purposes have been shown to introduce error.[80,81] Second, diagnostic codes collapse audiometric data down to two discrete groups, those with and without hearing loss, preventing the reporting of hearing loss by frequency and severity (mild, moderate, severe). Third, estimates of prevalence using diagnostic codes is conditioned on Veterans having had a hearing test as part of a clinical visit. A Veteran's decision about whether to visit an audiology clinic is likely based on idiosyncratic and complex factors. Accordingly, the absence of a hearing test does not mean absence of hearing loss, which impacts calculations of prevalence. Finally, previous studies reporting prevalence of hearing loss, while restricted to Veterans having served in post-9/11 conflicts, did not control for the length of time since service. Therefore, prevalence estimates of hearing loss could be reflecting hearing loss attributable to not only military service but also to non-military occupational and recreational exposures since service. Estimates of the number of Veterans with hearing loss and the degree of hearing loss entering the VA health care system is necessary to inform policy makers and providers about potential audiologic resource utilization and projected costs for early intervention.

Estimates of hearing loss prevalence for those in military service could help illuminate the potential burden on VA hearing health services. For example, in 2018, the DoD estimated the prevalence of hearing loss among Service members enrolled in a hearing conservation program to be 15%; estimates varied by service branch and component.[67] Hearing loss was defined as any test frequency (250-6000 Hz) with a threshold > 25 dB HL. However, Service members enrolled in this hearing conservation program may not be representative of the general Service member population nor of Service members who transition to Veteran status and use the VA for their healthcare. Additionally, despite having audiometric thresholds, the DoD reported only whether hearing loss was present (yes/no) and did not elaborate on the severity of hearing loss these Service members were experiencing.[67] There remains a gap in our understanding of the hearing loss burden, and the degree of loss, among recently separated Veterans entering the VA health care system.

2.6. Rate of hearing change during military service

Since the IOM report, the DoD has encouraged the testing of all Service members' hearing at entry into military service and again when exiting service.[82] The occurrence of audiometric surveillance during military service is related to deployments and military occupations in known noisy work environments.[83,84] As such, most Service members now receive two or more hearing tests during their military service. An example audiogram from a single individual (one ear) tested at two time points (time point one with solid circles and time point two with dashed circles) is shown in Figure 2.2. The audiogram is a plot of pure tone thresholds in dB hearing level (dB HL) as a function of test frequency (Hz). Thresholds plotted above the red line suggest normal hearing and below the red line, impaired hearing, for that frequency. As with most occupational hearing conservation programs, hearing change in the military is measured as a significant threshold shift (STS).[83] An STS is a clinically meaningful hearing change compared to a baseline hearing test. Specifically, STS is defined as a change in hearing by 10 dB or more in the average of hearing thresholds at test frequencies 2, 3, and 4 kHz.[67,84,85] Significant threshold shifts can occur within the normal range of hearing or occur within an already impaired ear.[66] Figure 2.2 is an example of STSs at 2000 Hz and higher.

Typical of STS reporting, meaningful hearing changes are reported as percentages of occurrence rather than actual magnitude of hearing change of frequencies impacted. For example, a recent report by the Army noted the incidence of STS diagnosis in 2013 was

1.7% and had remained relatively constant from 2009-2013.[65] While repeat cross-sectional views of the number of Service members or Veterans with hearing loss over time can yield information about how the groups change from year to year, it cannot be used to summarize individual-level hearing changes within a year's time.

Figure 2.2. Example audiogram

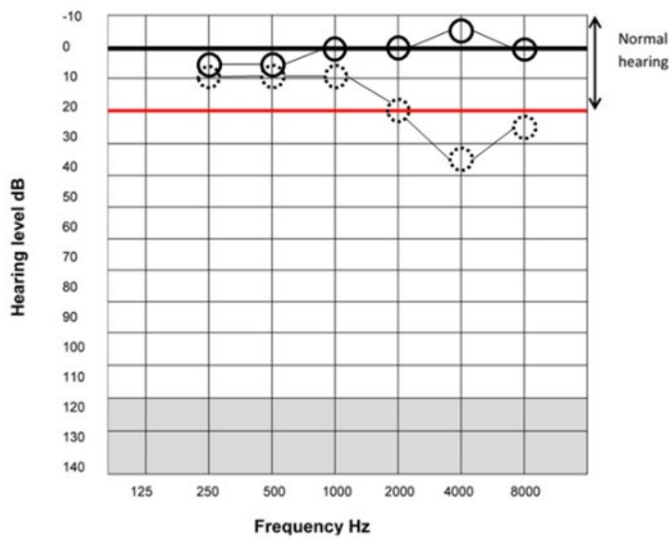

Figure legend: Plotted are the pure tone thresholds for one ear at two time points for an individual. The solid circles represent time point one and dashed circles time point two. In this example, the individual would be considered to have had a significant threshold shift, but the magnitude, frequency, and time occurrence would be lost.

Hearing sensitivity exists on a continuum. Clinically defined normal hearing spans a range of approximately -10 to 25 dB HL and hearing loss spans a range from 25 to about 110 dB HL. Thus, the range of 'normal' is approximately 35 dB. This wide range allows for substantial hearing changes to occur without an individual ever being diagnosed as having hearing loss. Similarly, hearing change exists as a continuum of severity rather than an all-or-none phenomenon. Thus, the real question in population studies of Service members is not "Did the Service member's hearing change during military service" but

"How much and how quickly does each person's hearing change over their military service period?" To date, no studies have estimated the rate of hearing change that occurs during military service. Determining the rate of hearing change and potential risk factors that affect the rate of change is important to elucidate the impact of military service on hearing. Because of the adverse communication and health outcomes associated with worsening hearing, studies using prospectively collected data from individuals in the recent post-9/11 conflicts are needed.

2.7. Increasing our understanding of how blast exposures lead to self-reported hearing difficulty among normal hearing Veterans

As discussed earlier, blast exposure is a known cause of hearing loss. Further, substantial evidence shows blast exposure is associated with self-reported hearing difficulty, especially in complex acoustic environments such as understanding speech in background noise, among Veterans *normal or near-normal* hearing in the audiogram.[14-16,29,63] The ability to listen and understand speech in complex acoustic environments like background noise depends critically on an intact auditory system, from cochlea to cortex. The ability to understand speech in complex acoustic environments also requires sustained attention and focus on the target signal, tasks which are largely outside the auditory system. Thus, mechanisms that affect attention and focus may result in perceptual hearing deficits and self-reported difficulty.[15] Two pathologies frequently observed among post-9/11 Veterans and that can interfere with sustained attention and focus are traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD). TBI was observed in 15-23% of returning Service members.[86,87] Similarly, 20% of returning Service members are affected with

PTSD.[88] Among Veterans, these two pathologies frequently co-occur, with 64-73% individuals with a diagnosis of TBI also having a co-morbid PTSD diagnosis.[89,90] It is also possible that exposure to blasts can result in PTSD without a TBI.[91] Therefore, considering the well-established pathway between military blast exposure and PTSD,[92] it is possible that the effects of blast on self-reported hearing difficulty is mediated through PTSD.

Individuals with PTSD subjectively complain about concentration, attention, and memory. Vasterling and Brailey suggested that PTSD is characterized by relatively less proficient initial acquisition of information and heightened sensitivity to interference.[93] Initial acquisition has been linked to the functional integrity of the prefrontal cortex and attention.[92] Additionally, Veterans with PTSD have shown weaknesses on tasks of working memory and sustained attention, but not on tasks of attentional shifting or selection of targets from an array.[93,94] Finally, trauma exposures have been linked to a range of adverse health outcomes, both objective and self-reported.[95-97] A conceptual framework has been proposed that links a trauma exposure to severe and persistent distress, primarily PTSD, which leads to psychological and attentional mechanisms resulting in altered symptom perception.[98] The distress, which increases allostatic load, is necessary to engage attentional mechanisms that can lead to poor health.[99,100] Thus, even if the blast exposure (traumatic event) does not lead to direct physical harm of the auditory system and subsequent hearing loss, blast exposure that leads to PTSD may result in self-reported hearing difficulty. Consequently, evidence is largely lacking on mediators linking blast to self-reported hearing difficulty and to the extent to which intervening on these mediators could mitigate blast disparities in perceptual deficits.

2.8. Contributions of this dissertation to the literature

The review above demonstrates the gaps in foundational knowledge and the need for research on hearing outcomes in Veterans of recent wars. We are lacking a valid estimate of the prevalence of hearing loss following service separation and the rate of hearing change during service. Furthermore, with increasing numbers of Veterans returning home having experienced a blast exposure, there is an urgent need to better understand reports of hearing difficulty in the audiometrically normal, but blast-exposed, population. Lack of information about hearing outcomes in the newest generation of Veterans represents a serious gap that prevents optimal care. Their deployment experience differs from that of Veterans of earlier war eras with respect to numerous factors, such as blast exposure and better likelihood of survival. Shifting the focus to recently returned Veterans spotlights opportunities for intervention in younger Veterans for whom adverse effects of hearing loss might be mitigated.

The overall goal of this body of work is to provide foundational data on military noise and blast exposure, and to establish its associations with auditory function (including mechanisms of action) among post-9/11 Service members and Veterans. Toward achieving this objective, this dissertation makes contributions in three areas: (1) the post-separation prevalence of hearing loss by severity among VA health care users; (2) rates of hearing changes by frequency during military service and as a consequence of occupational noise exposure; and (3) the effects of blast exposure on self-reported hearing difficulty via PTSD in audiometrically normal hearing Veterans. The work that follows is directly responsive to the IOM call for research on hearing outcomes in Service members and Veterans. Each of these dissertation aims was investigated using unique administrative databases, prospectively collected data, and using novel analytical approaches described in the individual dissertation chapters.

In Aim 1 we estimated the prevalence of mild, moderate, and severe hearing loss among Veterans who have recently separated from the military and who use VA health care. This aim provides the first estimate of the national prevalence of hearing loss by severity among Veterans of post-9/11 wars who use VA health care. Knowing the prevalence of hearing loss is required for the VA to plan appropriate resource allocation for hearing health care services for Veterans. In Aim 2 we estimated the average change in Service members' hearing over the course of military service as a consequence of military occupational noise exposure ranking. This aim leveraged Service members' audiometric data collected as part of the DoD hearing conservation program to determine the average change in hearing thresholds by frequency over time, which is a unique use of DoD data. This was the first analysis of hearing change over time using such data and adds to the limited literature on frequency-specific hearing outcomes during military service. Estimating the rate of hearing change by frequency, and risk factors that impact hearing, will inform DoD efforts to protect Service members' hearing during their military service. In Aim 3, we estimated the effects of blast exposure on self-reported hearing difficulty, and the mediating effects of PTSD on this relationship. Using regression models and following a formal causal mediation framework, we estimated total associations between blast exposures and hearing difficulty, natural direct and indirect associations, and percent of the observed associations mediated through PTSD. Moving from associations toward causality and mechanistic understanding is essential to both the prevention and rehabilitation of self-reported hearing difficulty. Given that blast exposures may not be preventable in all cases, an improved understanding of the mechanisms that cause those with blast exposure to report hearing difficulty could highlight opportunities for targeted interventions.

Chapter 3. A Bayesian Approach to Estimating Prevalence of Hearing Loss in Post-9/11 Veterans using VA Health Care

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Author Contributions: All authors contributed to this work. Kelly Reavis conceived of the study, performed the statistical analysis and wrote the manuscript. Dr. McMillan guided and assisted with the statistical analysis, interpretation of the statistical findings, and critical review of the manuscript. Dr. Henry designed the prospective research study used in the prediction model and critically reviewed the manuscript. Dr. Snowden assisted with interpretation of the findings and critically reviewed the manuscript. Dr. Carlson assisted with and supervised all aspects of the study and critically reviewed the manuscript; she also designed the prospective research study used in the prediction model.

3.1. Abstract

3.1.1. Objective

To estimate the prevalence of mild, moderate, and severe hearing loss among post-9/11 Veterans who have recently separated from the military and who use the Veterans Affairs (VA) health care system for their primary or mental health care. This estimate is critical for audiologic service resource allocation and planning. Estimation of the burden of hearing loss requires measurement of hearing thresholds. However, because not all Veterans are tested, such data are not readily available. To overcome this gap, we leveraged administrative healthcare data along with primary data collected in Veterans and employed a novel estimation technique.

3.1.2. Data Sources

The data sources were VA health care administrative data and research data from the Noise Outcomes in Servicemembers Epidemiology (NOISE) Study, a prospective cohort study conducted within the VA Portland Health Care System. The study sample included Veterans who separated from the military between August 2011 and August 2017.

3.1.3. Study Design

The study used a cross-sectional design. The primary outcome was hearing loss severity (none, mild, moderate, or severe hearing loss) across the speech frequency range (500-4000 Hz). Predictors of hearing loss severity included age, sex, and military service branch. We used Bayesian logic within a multilevel regression model with poststratification to estimate the prevalence of hearing loss.

3.1.4. Data Collection/Extraction Methods

Audiometric hearing thresholds measured within 2.5 years of military service separation were extracted from the VA health care records of post-9/11 Veterans. Similar hearing threshold data were collected from Veterans enrolled in the NOISE Study. All Veterans were classified as either having a clinical hearing test or not.

3.1.5. Principal Findings

Only 18% of the VA sample had hearing tests. Based on model results, we estimated the prevalence of hearing loss among all Veterans in the target population to be 10.6% (90% credible intervals: 7.8%-19.9%). Most hearing loss was mild.

3.1.6. Conclusions

There is a high burden of hearing loss among recently separated post-9/11 Veterans who use VA healthcare. Mild hearing loss can impose difficulties in everyday life, and when present during early life years can culminate in reduced functioning and quality of life during older ages. Therefore, it is imperative that we investigate structural interventions and secondary or tertiary prevention strategies to mitigate the consequences of hearing loss.

3.2. Introduction

We aimed to estimate the prevalence of mild, moderate, and severe hearing loss among post-9/11 Veterans who have recently separated from the military and who use the Veterans Affairs (VA) Health Care System. This is important to the VA because despite hearing conservation efforts, military Service members remain at risk for developing service-related hearing loss requiring post-service diagnosis, rehabilitation, and potential disability compensation, placing a burden on the VA health care system. Untreated hearing loss is associated with increased health care costs and is a risk factor for common and costly diseases such as dementia.[101,102] There are also social and economic costs for individuals with hearing loss. A widespread intervention in the VA health care system to mitigate the human and financial costs of hearing loss, such as aural rehabilitation, is necessary especially among post-9/11 Veterans for whom the consequences of hearing loss might still be prevented. However, there are currently no estimates of the number of Veterans with hearing loss coming into the VA health care system to inform policy makers and providers about potential audiologic resource utilization and projected costs for early intervention.

Prevention and early intervention are strategic goals of the VA. Of particular interest are the hearing health needs of post-9/11 military Veterans because they self-report serious difficulty hearing more readily than Veterans of other war eras.[74] Moreover, a large proportion (62%) of post-9/11 Veterans use VA health care and an increasing percentage of VA health care users are post-9/11 Veterans,[103] which translates to increased health care spending on this population. Preparation and resource planning for a widespread hearing health care intervention in this population requires an understanding of the prevalence of the problem among Veterans using VA health care. Specifically, estimates of the prevalence of hearing loss by severity are needed because practice standards vary by degree of impairment. For example, treatment for mild hearing loss may include a low gain hearing aid while severe hearing loss may necessitate a cochlear implant to restore audibility and clarity of the speech signal.

Over 4.8 million people have served in the military since 9/11.[17] The total number of individuals who experienced hearing loss by the time their service ended may be substantial.[9] A congressionally mandated and VA sponsored Institute of Medicine (IOM, now known as The Health and Medicine Division of the National Academies) report published in 2006 noted a considerable knowledge gap in our foundational understanding about the epidemiology of hearing loss in the military and its consequences for VA health services.[9] In a comprehensive review of the literature, the IOM reported most hearing loss data were derived from small or highly selective study samples that precluded interpretations of hearing loss prevalence at service separation among Service members.[9] Furthermore, it raised questions about the generalizability of these findings to the VA health-care-using population. Since the release of the IOM report, epidemiologic efforts to quantitatively describe the prevalence of hearing loss have been slow. This fundamental knowledge about hearing could inform allocation of financial and human resources to guide VA care, military service-related rehabilitation, and disability compensation services.

Historically, approaches to estimate the prevalence of objective hearing loss include extracting diagnostic codes or disability claims from administrative health care databases. To date, two studies have investigated the prevalence of hearing loss among post-9/11 Veterans using diagnostic codes; Frayne et al[78] and Swan et al[79] reported prevalence estimates of 19% and 13%, respectively. The VA, using disability claims, estimated that hearing loss was the 10th most prevalent service-connected disability, affecting 2.1% of the post-9/11 population.[77] Disability claims are present for Veterans who file for disability benefits for health conditions related to their military service. The VA applies a strict definition of hearing disability, which likely explains the difference in estimates of the prevalence of hearing loss between diagnostic codes and disability claims. Disability claims will not represent cases of more mild hearing losses whereas diagnostic codes will generally capture any hearing loss regardless of severity.

The use of diagnostic codes and disability claims to estimate prevalence is limiting in two ways. First, diagnostic codes collapse audiometric data down to two discrete groups, those with and without hearing loss, preventing the reporting of hearing loss by severity (mild, moderate, severe). Second, estimates of prevalence using diagnostic codes and/or disability claims require Veterans to have had a hearing test as part of a clinical visit. Although the use of electronic health record data to estimate hearing loss prevalence for measuring and monitoring Veteran population hearing health is more cost-effective than conducting hearing assessments in the population, electronic health record data only include a small, non-random subset of Veterans who sought audiologic evaluation. A Veteran's decision about whether to visit an audiology clinic is likely based on idiosyncratic and complex factors. Accordingly, the absence of a hearing test does not mean absence of hearing loss, which impacts calculations of prevalence. As such, diagnostic codes and disability claims cannot be relied upon to estimate the number of individuals who, entering the VA health care system, may present to VA audiology clinics for services if a structural intervention were applied. Obtaining VA population-level health estimates of the prevalence of mild, moderate, and severe hearing loss requires different approaches than what have been taken historically.

In the present study, we estimated the prevalence of hearing loss by severity among all recently separated Veterans using VA health care between August 2011 – August 2017, given that some Veterans were not tested.

3.3. Methods

3.3.1. Overview

The target population for this study is recently separated post-9/11 Veterans who use VA health care. The study sample includes post-9/11 Veterans who have used VA health care for their primary care or mental health care within 2.5 years of military service discharge and who separated between August 2011 and August 2017 (the 'VA-user sample,' described further below). Estimating the prevalence of hearing loss by levels of severity requires extraction of audiometric hearing threshold data. For those Veterans in the VA-user sample who had been seen in audiology, audiometric data could be extracted from VA administrative health care records. For those who had not been seen in audiology, no audiometric data are available and thus their hearing thresholds must be predicted. To derive predicted hearing thresholds, we used audiometric data from a research study in which characteristically similar Veterans were enrolled (the 'NOISE Study sample,' described further below). Hearing loss severity, determined by one's hearing thresholds, was then assigned to each Veteran in the VA-user sample using either actual VA audiologic data or predicted hearing thresholds based on NOISE Study data. We then combined the observed hearing loss severity counts from those seen in audiology with the predicted hearing loss severity counts from those without audiology visits to derive estimates of the prevalence of hearing loss by severity for the VA-user sample. Inferences from this sample may then be used to predict and plan for hearing health care needs for more recent newly separated post-9/11 Veterans who use VA care.

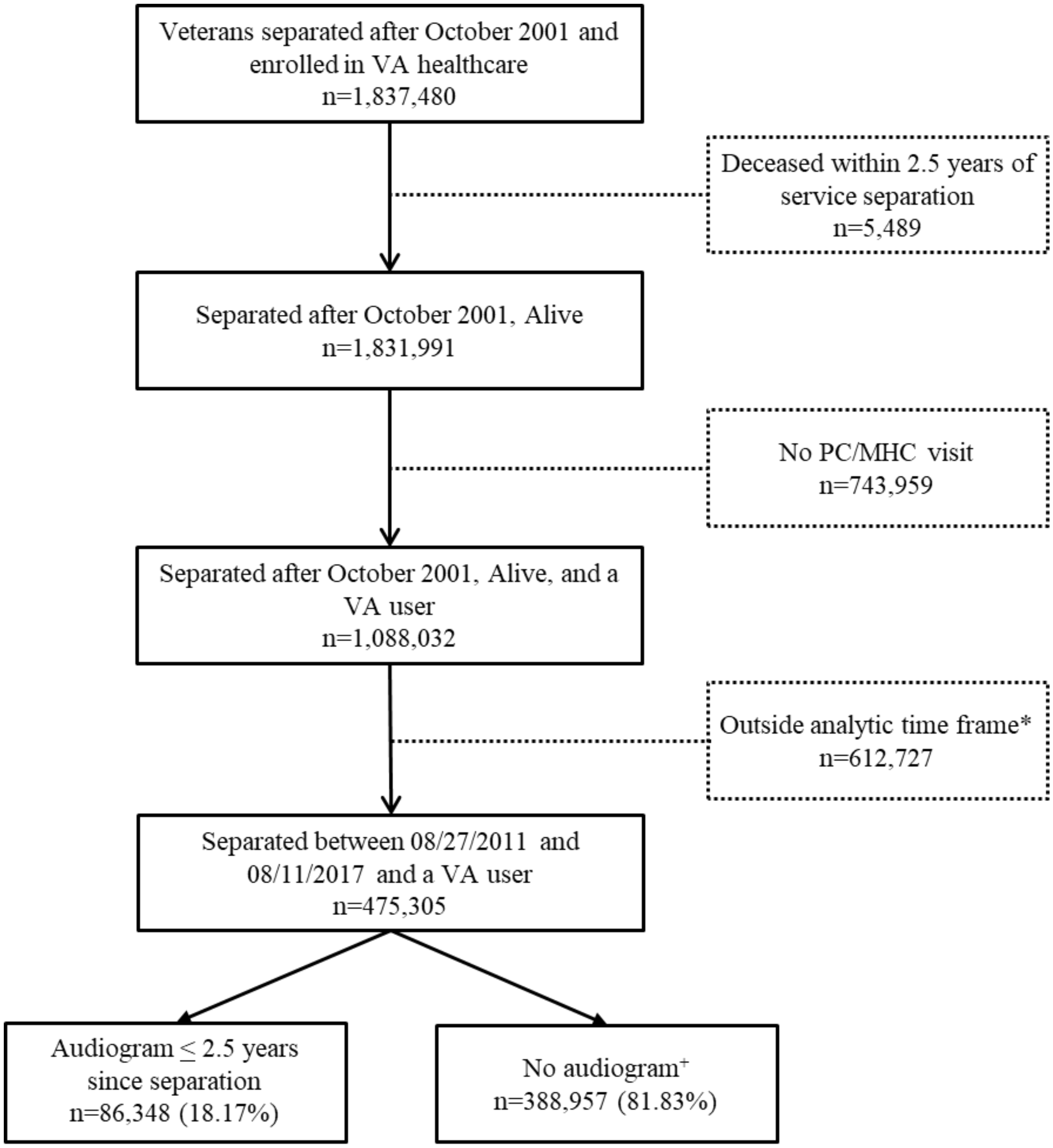
3.3.2. Data Sources

VA-user Sample. We used the VA/DoD Identity Repository (VADIR) to secure a list of all Veterans who have served since October 2001 and have separated from the military.[104] October 2001 coincides with the beginning of Operation Enduring Freedom and the United States invasion of Afghanistan in response to the September 11th attacks and marks the beginning of the post-9/11 service era. This sampling frame was linked with the VA Corporate Data Warehouse (CDW) using social security numbers to identify post-9/11 Veterans with a VA health care record (n=1,837,480). The VA CDW database is a large-scale relational data warehouse that draws from numerous clinical and administrative systems for all VA-enrolled Veterans and provides a nationwide view of all information entered into the electronic health record of the patient.[105] When a Veteran receives a hearing evaluation in the VA health care system, the audiologist reports the patient's information to a hearing loss repository. Data from the hearing loss repository are then shared with the VA CDW.

Service separation date, vital status, health care utilization, and audiometric data were extracted from Veterans' health care records. Veterans deceased within the 2.5 years of service separation were excluded (removing n=5,489). Veterans were defined as a health care user if they had a primary care or mental health care visit within 2.5 years of service separation. We applied this exclusion criterion (removing n=743,959) because we were interested in Veterans who are likely to use the VA as their primary health care service provider, including audiology services. Finally, the target sample was further restricted to a time frame of August 2011 to August 2017 (removing n=612,727). This time period overlapped with NOISE Study data collection and allowed 2.5 years of follow-up time between service separation and data extraction (February 2020).

Our final analytic sample included 475,305 Veterans. Veterans in the sample were then identified as either having a VA clinical hearing test within 2.5 years of service separation or not having a VA clinical hearing test, providing an estimate of the prevalence of hearing loss close in time to military separation. In our sample of VA health care using Veterans, 86,348 had a VA clinical hearing test (18.2%), and 388,957 did not have a VA clinical hearing test within 2.5 years of service separation (81.8%). The assembly of our VA sample is shown in Figure 3.1.

Figure 3.1. Schematic of sample.



*Time frame = 08/27/2011-08/11/2017 to correspond to NOISE Study data collection.
+Includes 29,866 Veterans with audiograms >2.5 years since service separation.
Abbreviations: PC/MHC, Primary Care/Mental Health Care

NOISE Study Sample. A prospective cohort study was used to provide information on post-9/11 Veterans without audiograms. The NOISE Study was designed to examine the longitudinal effects of military and nonmilitary exposures on auditory functioning among post-9/11 Service members and Veterans.[106] Individuals are eligible to participate in the NOISE Study if they remain currently enlisted or are within 2.5 years of military separation. The NOISE Study is a multisite study with data collection ongoing in Portland, Oregon and San Antonio, Texas. Study participants enrolled at the Portland site are primarily Veterans seeking VA health care from the VA Portland Health Care System. Study participants enrolled at the San Antonio site are primarily Active Duty Service members stationed at the Joint Base San Antonio. For the purpose of this analysis, only Veteran study participants enrolled in Portland, Oregon were included. Study enrollment commenced in early 2014 and consequently includes Veterans who separated from military service since August 2011. All study participants undergo an audiologic evaluation. All data are double entered into a database and cross checked for errors.[106] Similar to the VA sample, the NOISE Study sample was restricted to individuals defined as VA health care users (n=476). Further details of the NOISE Study can be found elsewhere.[106] In the NOISE Study sample, 98 (20.59%) had a VA clinical hearing test and 378 (79.41%) did not have a VA clinical hearing test prior to enrollment in the NOISE Study (informing the model used to predict the hearing levels of the VA-user sample without an audiogram).

This study was exempt from Institutional Review Board review and a waiver of informed consent and HIPAA authorization was granted by the Research and Development

Committee at the VA Portland Health Care System. Veteran data from the NOISE Study were shared via an Institutional Review Board approved data use agreement (Appendix A.1).

3.3.3. Outcome Variable

The primary outcome was hearing loss by severity. Hearing evaluations, both in VA audiology clinics and in the NOISE Study, were conducted in a sound treated booth by a licensed audiologist or trained technician. The testing protocol, test environment, and test equipment met ANSI S3.6 – 1996 standards.[107] Pure tone hearing thresholds were obtained at standard audiometric frequencies (250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz). From the thresholds, a pure tone average (PTA) was calculated at 500, 1000, 2000, and 4000 Hz.[108] The PTA of the worse ear was used to categorize the Veteran as having normal hearing (PTA ≤25 dB HL), mild hearing loss (PTA 26-40 dB HL), moderate hearing loss (PTA 41-60 dB HL) or severe to profound hearing loss (PTA ≥61 dB HL).[108] The worse ear was chosen because any noticeable problem may drive a Veteran to seek out audiology services.

The VA clinical audiograms were occasionally incomplete or with errors. Since 500, 1000, 2000, and 4000 Hz were necessary to determine hearing loss severity, any audiogram that was missing more than one threshold at these frequencies in either ear (<2% of the sample) was excluded. To remove data errors, data repair methods were used (described in detail in Appendix B). Another unique feature of the administrative audiometric data was the presence of multiple (repeat) audiograms conducted on the same day. If repeat audiograms were identified, the retest was used rather than the original. If only selected frequencies were retested, then thresholds from the retested frequencies were used in combination with the thresholds from the original audiogram.

3.3.4. Independent variables

The following variables were extracted for use as demographic covariates in multilevel modeling: age at the time of service separation (≤19, 20-29, 30-39, 40-49, ≥50), sex (male, female), and service branch (Army, Air Force, Navy, Marine Corps, Coast Guard). These variables were chosen because they are known risk factors for hearing loss. Together, these three variables led to 50 (5 x 2 x 5) unique demographic subtypes, also referred to as poststratification cells.

3.3.5. Statistical Analysis

We partitioned the VA-user sample into 2 groups: Veterans who had a clinical hearing test and Veterans who did not have a clinical hearing test. To estimate the prevalence of hearing loss for the entire sample, we used the following formula: Let p_k denote that prevalence at the kth severity level of hearing loss, k=1 to 4 corresponding to None, Mild, Moderate, and Severe. We define a binary indicator H_k for each Veteran corresponding to presence or absence of the kth hearing loss level in that person for which we have an audiogram and define R_k as the predicted binary indicator of the kth hearing loss level in a person who had *not* been tested. The prevalence of interest is defined as $p_k = \frac{\sum H_k + \sum R_k}{n+m}$ where n is the total number of Veterans in the VA-user sample with an audiogram, m is the total number of Veterans in the VA-user sample without an audiogram and the sum is over Veterans in the sample with hearing loss severity, k. H_k

can be estimated from the VA administrative database, containing health care records for all Veterans receiving care. Although R_k cannot be directly estimated by existing health care databases, it was informed through prospectively collected research data untethered to clinical care.

Predicted R_k was estimated using multilevel regression and poststratification (herein abbreviated as MRP).[109] The general idea of MRP is to estimate the PTA within each poststratification cell using a multilevel model and then using the model-based parameter estimates to predict the PTA among Veterans who have not had a hearing test. Poststratification is a method for correcting for known differences between the sample and population to which we wish to extend our findings.[110]

We used Bayesian multilevel regression to model individual audiometric PTAs as a function of demographic covariates among Veterans enrolled in the NOISE Study. The study sample was restricted to those Veterans without a VA clinical audiogram prior to enrollment in the NOISE Study (n=378). The PTA responses Y were fit to a multilevel model of the form:

$$y_i \sim N\left(\mu + \alpha_{j[i]} + \beta_{k[i]} + \gamma_{l[i]} + (\alpha\beta)_{jk[i]} + (\alpha\gamma)_{jl[i]} + (\beta\gamma)_{kl[i]} + (\alpha\beta\gamma)_{jkl[i]}, \sigma_y^2\right),$$

$$\text{for } i = 1, \ldots n$$

$$\alpha_j \sim N(0, \sigma_\alpha^2), \text{ for } j = 1, .., J$$

$$\beta_k \sim N\left(0, \sigma_\beta^2\right), \text{ for } k = 1, .., K$$

$$\gamma_l \sim N\left(0, \sigma_\gamma^2\right), \text{ for } l = 1, .., L$$

Parameters α_j, β_k, and γ_l are the random effects for the categorical covariates age, sex, and branch of service, respectively (and their two-way and three-way interactions). All random effects were modeled using independent normal prior distributions with a mean of zero, for example, $\alpha_{j[i]}^{age} \sim N(0, \sigma_{age}^2)$. A key advantage to multilevel regression is the inclusion of these random effects, which assumes the different levels of a covariate are related to each other with a common variance. Thus, a multilevel model with random effects will partially pool the different levels of a covariate parameter estimate toward its mean, with the degree of pooling determined from the data. Greater pooling occurs when the sample size is small and when the variance between categories within the covariate is small. Larger sample sizes have more information, so the corresponding multilevel estimates are closer to the individual level averages within a covariate. Generally, estimates for sparse poststratification cells are improved by borrowing information from demographically similar cells with more data.[109,111-113] Random effects statistically account for the age-, sex-, and service branch-level correlations among individual observations in the model-fitting; epidemiologically, they represent age-, sex-, and service branch-level contextual effects on hearing.

The above model precludes deriving the posterior distribution in an algebraic form.[114,115] Therefore, Markov Chain Monte Carlo (MCMC) methods, with the No-U-Turn sampling algorithm and 1,000 iterations, were used to obtain the posterior distributions of the model parameters. Next, for each parameter vector simulated from the posterior distribution of the model parameters, we predicted the PTA for each Veteran in the untested VA sample. This process of taking random draws from the posterior distribution of the parameters and then predicting each individual's PTA given those parameters was repeated 1,000 times to give an approximation of the posterior predictive distribution for each Veteran. The samples were indexed by sample iteration i, so that the percentages were also indexed, i.e.:

$$p_k^{(i)} = \frac{\sum H_k + \sum R_k^{(i)}}{n+m}.$$

A histogram of $p_k^{(i)}$ over all sample iterations is an estimate of the posterior distribution of p_k, providing the estimated prevalence of each hearing level among the population of VA health care-using Veterans (both those who received audiograms and those who did not). Finally, we repeated this model and subsequent predictions by taking the natural log of the PTA to increase the accuracy of right-skewed data predictions (i.e., elevated PTAs consistent with moderate and severe hearing loss).

3.4. Results

The overall demographics of the VA-user sample (n=475,305) and the NOISE Study sample (n=476) are displayed in Table 3.1. The VA-user sample included primarily men (86.4%) and about half (48.5%) of the sample participants were between the ages of 20 and 29 years. Additionally, 58.5% of the sample had served in the Army; only 0.2% were Coast Guard Veterans. Of this sample, 18.2% had a VA hearing test. The NOISE Study sample was largely similar to the VA sample in the distribution of demographic characteristics and the proportion who had a hearing test.

Table 3.1. General characteristics by data source.

Characteristic	VA-user Sample (n=475,305)	NOISE Study Sample (n=476)
	N (%)	N (%)
Age (years)		
< 19	414 (0.1)	2 (0.4)
20-29	230,635 (48.5)	243 (51.1)
30-39	128,279 (27.0)	117 (24.6)
40-49	91,664 (19.3)	84 (17.7)
50 +	24,313 (5.1)	30 (6.3)
Sex		
Male	410,797 (86.4)	395 (83.0)
Female	64,508 (13.6)	81 (17.0)
Service Branch		
Army	278,216 (58.5)	227 (47.7)
Marine Corps	62,265 (13.1)	76 (16.0)
Navy	65,484 (13.8)	83 (17.4)
Air Force	68,467 (14.4)	79 (16.6)
Coast Guard	873 (0.2)	11 (2.3)
VA Clinical Hearing Test		
No	388,957 (81.8)	378 (79.4)
Yes	86,348 (18.2)	98 (20.6)

The distribution of the proportion of Veterans with observed hearing loss (PTA in the worse ear >25 dB HL) and mean PTA (dB HL) by age, sex, and service branch is presented in Table 3.2. The table is stratified by data source (VA-user sample vs. NOISE Study sample) and by the presence (yes/no) of a clinical hearing test. Among the VA sample, the proportion with hearing loss and mean PTA is absent from those without a clinical hearing test within 2.5 years of service separation, as expected. Additionally, the sample size is the smallest, and sometimes missing completely, among Veterans ≤19 years of age and among Coast Guard Veterans. The proportion of Veterans with hearing loss among demographic subtypes ranged from 0% to 60% (some data not shown due to small sample sizes and risk to patient confidentiality) and the mean PTA ranged from 6.3 dB HL to 25.6 dB HL. Generally, men had a higher prevalence of hearing loss compared to women (17% vs 9.3%) and prevalence of hearing loss and mean PTA increased with each age group. Among men, Army Service members had the highest prevalence of hearing loss and the highest mean PTA within each age group. However, among women, no pattern by service branch was observed. Overall, among those in the VA sample with a hearing test (n=86,360), the prevalence of any hearing loss was 15.9% (n=13,743). Most Veterans had mild hearing loss. The prevalence of mild, moderate, and severe hearing loss was 12.6%, 2.7%, and 0.7%, respectively.

Among the NOISE Study sample, the proportion with hearing loss and mean PTA is available for those both with and without a clinical hearing test because of their participation in the research study (Table 3.2). However, due to the sample size of the NOISE Study, there are few Veterans within each unique demographic subtype—especially few representing the youngest (≤19 years old) and the oldest (≥50 years) Veterans and Coast Guard Veterans. An underlying assumption is that the NOISE Study sample is sufficiently similar to the VA-user sample such that it can be used to predict the PTA in the VA-user sample without a clinical hearing test. To test this assumption, we compared the mean PTA values among the NOISE Study sample with a clinical audiogram to the VA sample with a clinical audiogram, focusing on the NOISE Study demographic subtypes with at least a sample size of 5 (Table 3.2). No large deviations were observed between the two data sources (the absolute difference varied by less than 3 dB), suggesting this was a reasonable assumption.

Table 3.2. Sample size (N), percent with hearing loss,[a] and mean PTA[b] by sample, sex, age group, service branch, and history of VA clinical audiogram.

Males		VA-user Sample							NOISE Study Sample						
		Clinical Hearing Test			No Clinical Hearing Test				Clinical Hearing Test			No Clinical Hearing Test			
Age Group	Service Branch	N	Hearing Loss	Mean PTA	N	Hearing Loss	Mean PTA	Total N	N	Hearing Loss	Mean PTA	N	Hearing Loss	Mean PTA	Total N
≤19	Army	16	13%	18.8	298			314	0			2	*	17.5	2
	Marines	4	*	14.4	7			11	0			0			0
	Navy	1	*	6.3	10			11	0			0			0
	Air Force	1	*	15.0	9			10	0			0			0
	CG	0			0			0	0			0			0
20-29	Army	18,545	15%	15.4	96,873			115,418	12	*	16.0	75	3%	12.6	87
	Marines	9,701	14%	15.2	32,305			42,006	11	*	12.3	38	3%	12.5	49
	Navy	3,712	8%	13.1	19,857			23,569	6	*	11.9	28	0%	11.9	34
	Air Force	3,293	7%	12.8	15,159			18,452	3	*	18.3	23	0%	12.0	26
	CG	27	0%	10.6	161			188	0			0			0
30-39	Army	11,578	22%	17.7	56,670			68,248	9	*	18.2	49	12%	16.2	58
	Marines	2,543	20%	17.1	9,082			11,625	1	*	12.5	11	*	15.5	12
	Navy	2,726	13%	15.4	11,661			14,387	1	*	12.5	16	*	13.3	17
	Air Force	3,137	13%	15.4	12,523			15,660	2	*	16.9	9	*	14.7	11
	CG	59	15%	16.4	183			242	1	*	13.8	1	*	18.8	2
40-49	Army	9,296	33%	20.7	37,083			46,379	10	*	18.0	25	12%	18.7	35
	Marines	1,116	28%	19.1	3,796			4,912	0			4	*	16.9	4
	Navy	2,671	24%	18.6	9,333			12,004	2	*	10.6	9	*	18.3	11
	Air Force	4,080	24%	18.5	12,151			16,231	8	*	20.9	10	*	19.3	18
	CG	80	26%	18.4	180			260	3	*	20.8	2	*	15.0	5
≥50	Army	3,332	55%	25.6	9,819			13,151	4	*	26.6	7	*	18.2	11
	Marines	148	41%	22.9	380			528	1	*	22.5	1	*	30.0	2
	Navy	659	44%	24.0	1,813			2,472	0			4	*	25.3	4
	Air Force	1,496	47%	24.1	3,126			4,622	2	*	23.8	4	*	27.5	6
	CG	38	47%	22.9	59			97	0			1	*	23.8	1
Males Total		78,259	16.6%	17.2	332,538			410,797	76	13.16%	17.1	319	7.21%	14.7	395

Females		VA-user Sample							NOISE Study Sample						
		Clinical Hearing Test			No Clinical Hearing Test				Clinical Hearing Test			No Clinical Hearing Test			
Age Group	Service Branch	N	Hearing Loss	Mean PTA	N	Hearing Loss	Mean PTA	Total N	N	Hearing Loss	Mean PTA	N	Hearing Loss	Mean PTA	Total N
≤19	Army	2	*	18.8	50			52	0			0			0
	Marines	0			1			1	0			0			0
	Navy	2	*	13.1	10			12	0			0			0
	Air Force	0			3			3	0			0			0
	CG	0			0			0	0			0			0
20-29	Army	1,484	8%	11.7	14,861			16,345	5	*	9.8	12	*	11.8	17
	Marines	331	5%	10.8	1,875			2,206	1	*	11.3	7	*	10.2	8
	Navy	1,017	7%	11.6	6,466			7,483	5	*	9.0	7	*	10.2	12
	Air Force	629	5%	11.3	4,314			4,943	3	*	7.9	6	*	11.7	9
	CG	5	*	22.0	20			25	0			1	*	5.0	1
30-39	Army	1,085	12%	13.4	8,545			9,630	3	*	15.0	6	*	15.8	9
	Marines	100	5%	11.4	621			721	0			1	*	10.0	1
	Navy	446	9%	12.8	2,909			3,355	1	*	5.0	3	*	9.6	4
	Air Force	591	6%	12.6	3,781			4,372	0			3	*	10.0	3
	CG	6	*	8.3	33			39	0			0			0
40-49	Army	903	21%	16.6	5,742			6,645	2	*	12.5	3	*	11.3	5
	Marines	45	22%	15.9	193			238	0			0			0
	Navy	284	24%	17.6	1,427			1,711	1	*	6.3	0			1
	Air Force	543	13%	14.9	2,725			3,268	0			3	*	11.7	3
	CG	3	*	13.8	13			16	1	*	15.0	1	*	15.0	2
≥50	Army	324	34%	20.8	1,710			2,034	0			3	*	16.3	3
	Marines	4	*	16.9	13			17	0			0			0
	Navy	96	36%	21.3	384			480	0			0			0
	Air Force	187	22%	18.5	719			906	0			3	*	25.0	3
	CG	2	*	15.6	4			6	0			0			0
Females Total		8,089	9.3%	13.6	56,419			64,508	22	9.09%	10.2	59	1.69%	12.4	81

Abbreviations: PTA, pure tone average; CG, Coast Guard

[a] Hearing loss yes/no defined as PTA in the worse ear > 25 dB HL

[b] PTA using 0.5, 1, 2, and 4 kHz in the worse ear

*To protect patient confidentiality, the proportion with hearing loss was redacted for cell sizes < 20

The NOISE Study sample without a clinical audiogram prior to entry into the research study was used to establish the posterior distribution of the model parameters necessary to predict the PTA in the VA sample without a clinical audiogram. Figure 3.2 is a summary plot of the predicted PTA from the multilevel normal errors model (black) and log-normal errors model (red) as a function of those model predictors. The estimates and their Bayesian 50% credible intervals (25-75th percentiles) and 90% credible intervals (5-95th percentiles) are displayed. As can be seen in the figure, all demographic subtypes have an estimated PTA within the normal range; however, the Bayesian intervals indicate that mild hearing losses (PTA 26-40 dB HL) remain probable especially for young Veterans (≤19 years) and older Veterans (≥30 years). Generally, the predicted PTA varied by age and sex, but less so by service branch.

Figure 3.2. Predicted PTA (dB HL, worse ear) as a function of service branch, sex, and age group.

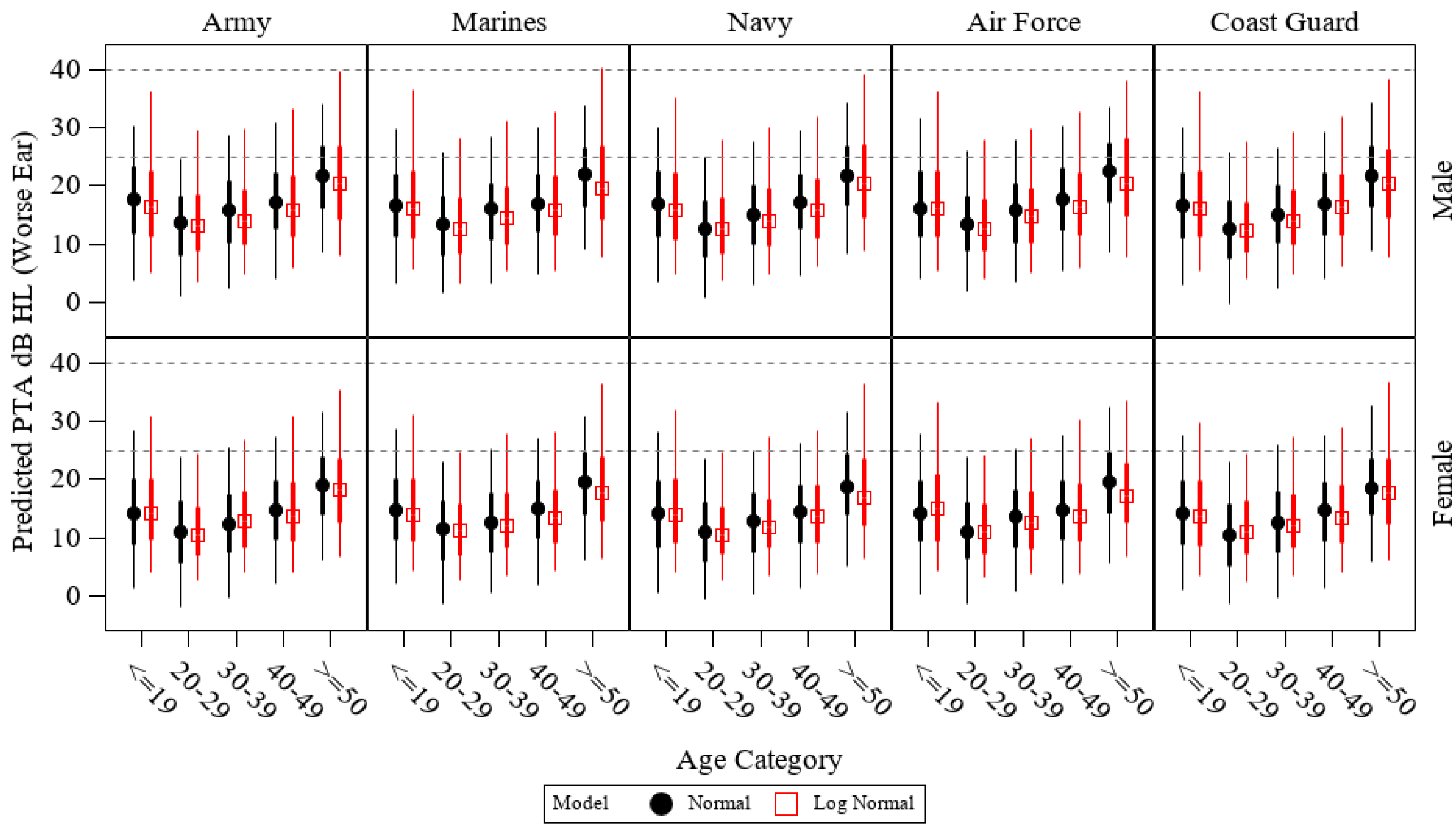


Figure legend: Circle and square markers indicate the 50th percentile of the posterior predictive distribution of the mean PTA for the normal model and log-normal model, respectively. Thin error bars reflect the 5-95th percentile range and the thicker error bars are the 25-75th percentile range of possible mean PTA values consistent with the data. Y-axis reference lines (grey dashed lines) are placed at 25 dB HL and 40 dB HL to show the cut point for mild and moderate hearing loss, respectively.

Abbreviations: PTA, pure tone average; dB HL, decibels hearing level

Next, we used that parameter vector, simulated from the posterior distribution of the model parameters, to predict the PTA for each Veteran (repeated over 1,000 iterations) in the untested VA-user sample. This Bayesian simulation approach has the added benefit of allowing us to compute functions of the parameters, such as the severity of hearing loss based on the estimated PTA, and therefore estimate the posterior predictive distribution of that function. Following simulation, each iteration of the predicted hearing loss severity was then summed across Veterans, including those Veterans with hearing tests to achieve a total count of Veterans with hearing loss (i.e., summed predicted and calculated). A histogram of overall sample iterations is the estimated posterior distribution of the prevalence of hearing loss by severity.

Figure 3.3 displays the posterior predictive distribution of the prevalence of hearing loss by hearing loss severity. Each panel shows the probability density function for the normal errors model (black, solid line) and the log-normal errors model (red, dashed line) as well as the estimates consistent with the 5th, 50th, and 95th percentiles of the distribution. The top panel reflects the prevalence of any hearing loss. The next three panels reflect the prevalence of hearing loss by severity: mild, moderate, and severe. We estimate the prevalence of any hearing loss among Veterans recently separated from the military who use VA health care to be 10.6% and we are 90% certain that the true prevalence ranges from 7.8-19.9%. The prevalence of mild, moderate, and severe hearing loss was estimated to be: 9.5% (90% credible interval: 6.9-16.7%), 1.0% (0.7-2.9%), and 0.14% (0.12-0.32%), respectively. It is obvious from these estimates that the vast majority of hearing loss is mild. While the estimated prevalence of hearing loss severity is similar between the two models, the log-normal model does estimate a slightly higher prevalence of moderate and severe hearing loss (1.0% and 0.14%, respectively) compared to the normal errors model (0.5% and 0.12%, respectively). Though these are incremental increases in the estimated prevalence, it reflects a doubling of the counts of Veterans with moderate and severe hearing loss. The observed prevalence of hearing loss based on the VA-user sample with hearing tests (Figure 3.3, vertical grey dashed line) fell within, although toward the upper bounds of, the Bayesian 90% credible interval for any severity of hearing loss and for mild hearing loss. However, the estimates for moderate and severe hearing loss from the VA-user sample with a hearing test were outside the estimated credible intervals.

Figure 3.3. Probability density function representing the range of prevalence values from the posterior predictive distribution

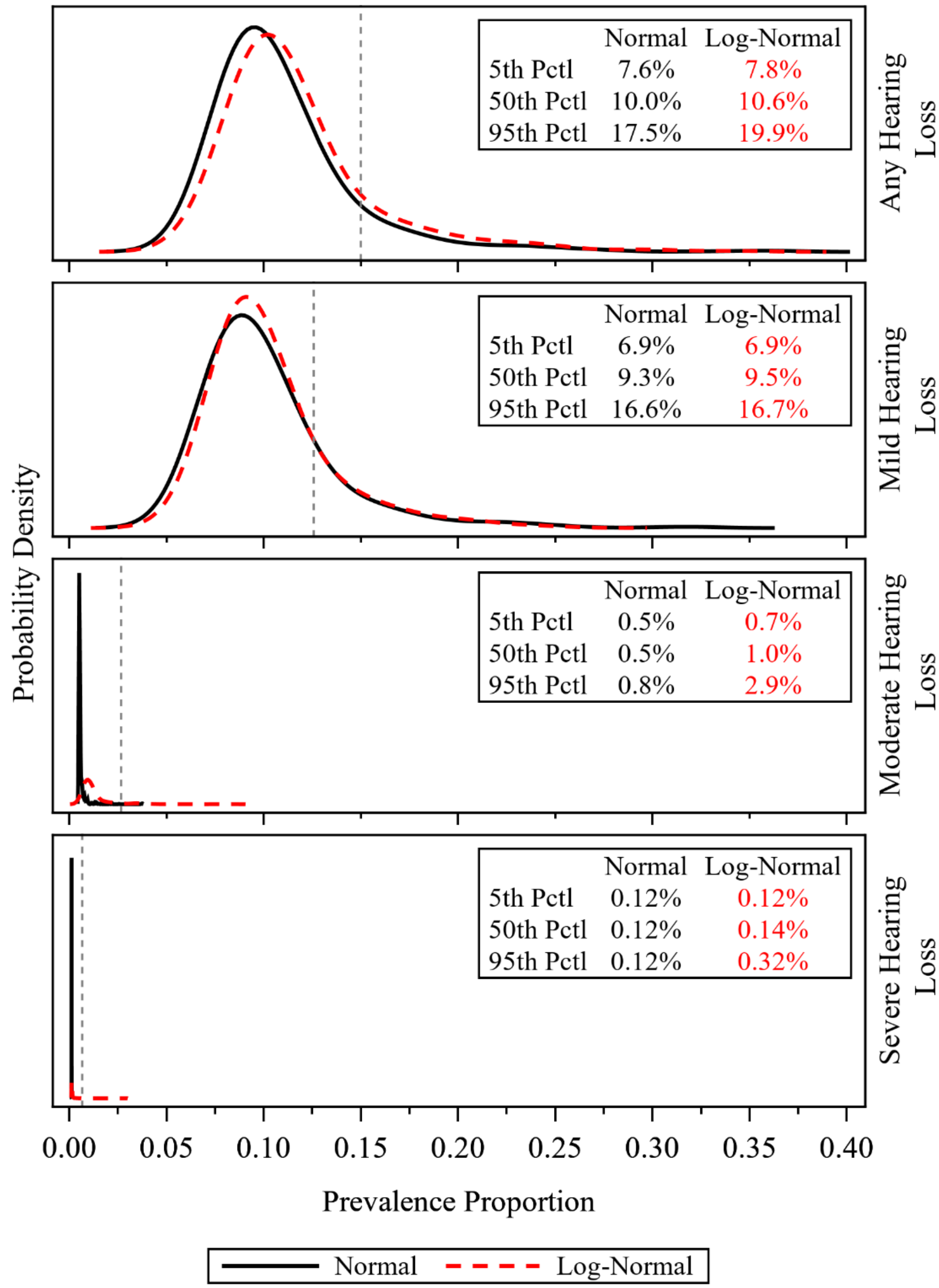


Figure Legend: Panels from top to bottom represent: Any Hearing Loss, Mild Hearing Loss, Moderate Hearing Loss, and Severe Hearing Loss. The 50th percentile prevalence estimate along the 5-95th range is displayed in each panel from the posterior predictive distribution. The dashed gray line indicates the prevalence estimate from the VA-user sample of Veterans with a hearing test.

3.5. Discussion

Hearing loss is a recognized problem in the VA health care system with a sizeable social and economic cost.[77] The extent of the hearing loss burden in the VA has been estimated, but not always well described or quantified. We used national VA hearing health care data and primary collected research data to estimate the prevalence of hearing loss by severity among a sample of Veterans, regardless if they had a clinical hearing test. Based on our results, we are 90% certain the true value of the prevalence of hearing loss (PTA >25 dB HL at 500, 1000, 2000, and 4000 Hz) lies between 8 and 20%, and our best approximation of prevalence is 10.6%, as estimated using Bayesian logic. Among those with hearing loss, the vast majority were mild, which was expected and consistent with other research in non-military occupations.[116] To our knowledge, this is the first study that quantified the prevalence of hearing loss by severity among all post-9/11 Veterans recently separated from the military and that use VA health care. This study highlights the high prevalence of hearing loss among Veterans coming into the VA health care system and the need for continued promotion of hearing health, hearing loss prevention efforts, and early intervention. This aligns with the Department of Veterans Affairs strategic plan to "anticipate the needs and provide quality benefits, care, and services" as individuals transition from military service to Veterans status.[117]

Given that only 18% of the VA-user sample had received a hearing test, our findings suggest that there is considerable potential for bias in prevalence estimates that rely solely on the availability of a clinical audiogram. Among Veterans with a hearing test, we observed 13,743 (15.9%) individuals with hearing loss. Considering 82% of Veterans did not have a hearing test, this is an undercount. However, the ability to extrapolate prevalence estimates to those in the VA-user sample without a clinical hearing test for the purposes of estimating the number of Veterans with hearing loss relies on the assumption that Veterans with a hearing test are like those without a hearing test. Put another way, health care records must be missing at random to generalize results to the broader VA-user sample. However, missing administrative health care records are not random and, often, records with more data are more representative of sick individuals than healthy ones.[118,119] To overcome this potential source of bias, we used a Bayesian approach within a multilevel framework. Doing so allowed us to produce a revised estimate of the prevalence of hearing loss and, thus, a more accurate estimate of the number of Veterans with hearing loss entering the VA health care system. A Bayesian prevalence estimate of approximately 10.6% suggests that 50,382 Veterans entered the VA with hearing loss over about a 6-year period (about 8,400 per year), although this figure could be as low as 37,074 or as high as 94,586. Given the high prevalence of hearing loss in this group of Veterans, this is potentially a substantial burden. Extracting only audiometric thresholds among those with a hearing test missed 63-85% of probable hearing loss cases.

Past estimates of the prevalence of hearing loss in post-9/11 Veterans derived from diagnostic codes ranged from 13% to 19%.[78,79] These previous estimates are within our estimated prevalence credible interval of 8-20%, although toward the upper end. In the absence of audiometric data, estimates of the prevalence of hearing loss derived from diagnostic codes could serve as an upper bound of the prevalence. Similarly, we observed greater prevalence of hearing loss in men than women, which is consistent with recent literature estimating the prevalence in post-9/11 Veterans.[78,79] As the number of women Veterans who seek VA health care services continues to increase in the years ahead, it stands to reason that the overall proportion of hearing loss among VA users will slightly decrease.

A natural extension of the model reported herein is the transportability to future Veteran cohorts entering the VA health care system. We used a Bayesian logic to provide a formal mechanism of combining sources of information to make predictions. The extent to which this model is accurate depends on the extent to which the population that we wish to predict and the population on which the predictions are based are similar. Furthermore, as long as the effects of age, sex, and service branch on hearing loss are the same, then this model can be used to predict the severity of hearing loss among future cohorts of Veterans that are lacking a clinical audiogram and summarized across Veterans to estimate the overall prevalence of hearing loss by severity.

3.5.1. Strengths and Limitations

Strengths of this study include the use of audiometric threshold data and a novel approach to estimate the prevalence of hearing loss in Veterans. We used multilevel regression with poststratification to maximize the utility of research data combined with electronic health record data to estimate the prevalence of hearing loss by severity in the entire user population. The multilevel regression with poststratification is applicable in many public health settings and can enable researchers to make better use of administrative data to facilitate insights into the prevalence of specific conditions and to improve services for those conditions. This method can help draw inferences about the population where data are sparse. To our knowledge, this approach has been used limitedly in public health and has never been used in hearing health.[112]

There are, however, limitations to the multilevel regression with poststratification approach and our application of it in this study. In the absence of exposure data and audiograms at the end of service, hearing impairment caused by military service can only be inferred. This inference was strengthened by limiting the audiogram to within 2.5 years of service separation. Another limitation is that our definition of hearing loss, though commonplace, is conservative. Our definition includes only audiometric frequencies up to 4000 Hz. Higher frequencies (6000 and 8000 Hz) are not included, which might have lowered the hearing loss prevalence estimates. Additionally, prevalence estimates of moderate and severe hearing loss are likely underestimates, with true prevalence likely higher than those shown here. Our log-normal errors model was implemented in an attempt to better capture the right-skewed nature of PTA data, but our estimates are still likely to be conservative. Finally, these models are difficult to externally validate. Hearing threshold data among all Veterans that allowed for direct estimation would be preferable, albeit logistically infeasible.

3.5.2. Implications

Knowing the number of Veterans with hearing loss by severity allows the VA to plan for resource allocation for hearing health care services for Veterans. Given the high prevalence of hearing loss in this group, there is likely substantial burden. We recommend that the VA investigate approaches to promoting healthy hearing among recently separated Veterans. From a clinical and rehabilitation perspective, mild hearing loss can impose difficulties in everyday life and mild hearing loss during early life years can culminate in decreased functioning and quality of life during older ages.[116] Hearing health promotion and hearing loss prevention strategies could include education, screening, and early intervention. Promotion efforts should include early discussions with Veterans about the importance of maintaining good hearing health. Efforts should also be placed on mitigating further hearing loss through early detection of hearing loss by annual audiometric testing and intervention. Although hearing loss is typically permanent, Veterans with hearing loss can benefit from aural rehabilitation mechanisms, such as hearing aids, and by adopting compensatory strategies to optimize communication.

Chapter 4. Occupational Noise Exposure and Longitudinal Hearing Changes in US Military Personnel

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Author Contributions: All authors contributed to this work. Kelly Reavis conceived of the study, performed the statistical analysis and wrote the manuscript. Dr. McMillan guided and assisted with the statistical analysis and interpretation of the statistical findings. Drs. Joseph and Snowden provided expert opinion and interpretive analysis. Dr. Henry, Dr. Carlson, and Ms. Griest designed the prospective research study and reviewed the data. All authors discussed the results and implications and commented on the manuscript at all stages.

4.1. Abstract

4.1.1. Objective

Auditory impairments, particularly those resulting from hazardous occupational noise exposures, are pressing concerns for the US Departments of Defense (DoD) and Veterans Affairs (VA). However, to date, no studies have estimated the rate of hearing-threshold change that occurs during service or how changes may vary by military occupation. Hearing-threshold changes during military service have historically been reported as the proportion of Service members demonstrating a significant threshold shift. This approach does not capture the rate of the hearing-threshold change or the specific audiometric frequencies impacted. Determining the rate of hearing-threshold change, and factors that affect the rate of change, is important to elucidate the impact of military service on hearing and to guide prevention strategies and subsequent hearing health care. Our primary objective was to estimate the annual rate of hearing-threshold change during military service as a consequence of military occupational noise exposure ranking.

4.1.2. Design

We linked audiometric data, collected from military personnel as part of a DoD hearing conservation program (HCP), to data describing demographic and military-service characteristics obtained from individuals enrolled in the Noise Outcomes In Servicemembers Epidemiology Study. The analytic cohort included Veterans who enlisted in military service after September 2001 (n=246). We examined the longitudinal association between military occupations categorized as having a low, moderate, or high

noise exposure ranking and pure-tone hearing thresholds (500-6000 Hz) using a hierarchical linear model. The average annual rate of hearing-threshold change and their 95% confidence intervals were estimated by service branch, military occupational noise exposure ranking, and audiometric test frequency.

4.1.3. Results

On average, hearing-threshold change ranged between -0.5 and 1.1 dB/year and changes over time varied by service branch, audiometric test frequency, and military occupation noise ranking. Generally, higher test frequencies (3000-6000 Hz) and military occupations with moderate or high noise exposure rankings had the greatest average annual rates of hearing-threshold change; however, no dose-response relationship was observed. Among Marine Corps personnel, those exposed to occupations with high noise rankings demonstrated the greatest average annual rate of change (1.1 dB/year at 6000 Hz). Army personnel exposed to occupations with moderate noise rankings demonstrated the greatest average annual rate of change (0.6 dB/year at 6000 Hz).

4.1.4. Conclusions

This study (1) demonstrates the unique use of DoD HCP data, (2) is the first analysis of hearing threshold changes over time using such data, and (3) adds to the limited literature on longitudinal changes in hearing. The difference in hearing-threshold changes across military branches is likely indicative of their varying noise exposures, hearing protection device use and enforcement, and surveillance practices. Results suggest Marine Corps and Army personnel are at risk for accelerated hearing-threshold changes and that, among

Army personnel, this is most pronounced among those exposed to moderate levels of occupational noise exposure. Estimates of the rate of hearing-threshold change by frequency and factors that impact hearing are useful to inform the DoD's efforts to protect the hearing of their Service members and to the VA's efforts to identify and rehabilitate those most likely to experience hearing-threshold change.

4.2. Introduction

This paper presents the estimates of the annual rate of hearing change during military service as a consequence of military occupational noise exposure ranking. This issue is important because hearing loss is often an unfortunate consequence of military service and is an important concern for the US Departments of Defense (DoD) and Veterans Affairs (VA). For active duty Service members, hearing loss makes it difficult to engage in war fighting and to perform job tasks, thereby impacting fitness for duty.[1,2] It is also associated with many adverse health outcomes including unintentional injuries, falls, social isolation, depression, cognitive decline, hospital readmissions, and increased health care costs.[3,25-28,30-32,34-36,120] In 2019, over 1.3 million Veterans were service connected for hearing loss and a portion received disability compensation, an economic burden for the VA health care system.[5] Hearing loss acquired during military service can lead to a lifetime of consequences for Service members and Veterans.[29] Understanding the longitudinal trends in hearing thresholds among military personnel may inform prevention and rehabilitation strategies, leading to increased quality of life.

Noise exposure is the primary cause of hearing loss among military personnel and it has been suggested that all military personnel will be exposed to hazardous levels of noise at some point during their time in service.[8] Acknowledging the risk of hearing loss and potential downstream consequences, the military engages in audiometric surveillance to abate and mitigate auditory injury.[83,121,122] The development of noise-induced hearing loss in the military has been described primarily on the basis of a calculation referred to as significant threshold shift (STS), a clinically meaningful hearing-threshold change compared to a baseline hearing test.[85,121] Meaningful hearing-threshold changes are reported as rates of STS occurrence. Population STS data are an important metric used for measuring the effectiveness of hearing conservation programs (HCPs). For instance, a report by the US Army noted the incidence rate of STS among Soldiers in 2013 was 1.7% per year and had remained relatively constant from 2009-2013.[65] No study to date has examined how slowly or rapidly hearing thresholds change at both an individual level or a population level in relation to military noise exposure. Rate of hearing-threshold change might be especially relevant, given the link between early noise exposures and accelerated age-related hearing loss later in life.[123,124]

The military consistently strives to improve its hearing conservation efforts. In general, the DoD is shifting away from audiometric surveillance of only individuals deemed 'at risk' for noise exposure to a broader population-health approach, encouraging the ongoing audiometric surveillance of hearing among all military personnel.[69,122] In part, this programmatic change is warranted due to the notion that all Service members will be excessively exposed to hazardous noise at some point during their military career.[8] However, there remain inconsistencies in various military strategies between service branches for HCP implementation and oversight, audiometric surveillance, and hearing protection.[125] For example, it has been suggested the hearing protection compliance and enforcement may vary based on noise exposure level, thus placing military personnel at risk for hearing-threshold changes.[125]

The aim of this study was to estimate the average annual rate of hearing-threshold change during military service for individuals enrolled in the Noise Outcomes in

Servicemembers Epidemiology (NOISE) Study and who served after September 2001.[106] Importantly, the analysis was designed to assess the variability in the average hearing-threshold change by occupational noise exposure. A deeper understanding of the rate of hearing-threshold change, and the factors that influence the development of hearing-threshold change, are important to clarify the impact of military service on hearing, guide preventions strategies, and administer subsequent care.

4.3. Methods

4.3.1. Data Sources

To estimate the annual rate of hearing change during military service, we require a dataset with details about military occupational noise exposure and audiometric thresholds collected over time. Such a dataset does not exist but can be constructed through the joining of two disparate data sources: (1) The NOISE Study, and (2) Defense Occupational and Environmental Health Readiness System - Hearing Conservation (DOEHRS-HC) data repository.

NOISE Study. The NOISE Study is a longitudinal investigation into the effects of military and non-military exposures on auditory functioning among post-9/11 Service members and Veterans.[106] Individuals are eligible to participate in the NOISE Study if they are active duty or within about 2.5 years from separation. Two sites are enrolling study participants, the National Center for Rehabilitative Auditory Research (NCRAR), located at the VA Portland Health Care System in Portland, Oregon and the DoD Hearing Center of Excellence on Joint Base San Antonio, in San Antonio, Texas; in the current study, only NCRAR-based participant data were used. Potential study participants were excluded if they did not serve post-9/11 or had been separated for more than 2.5 years from military service. Study participants undergo a comprehensive audiologic assessment and complete numerous questionnaires measuring demographics and relevant military and non-military exposures.[106]

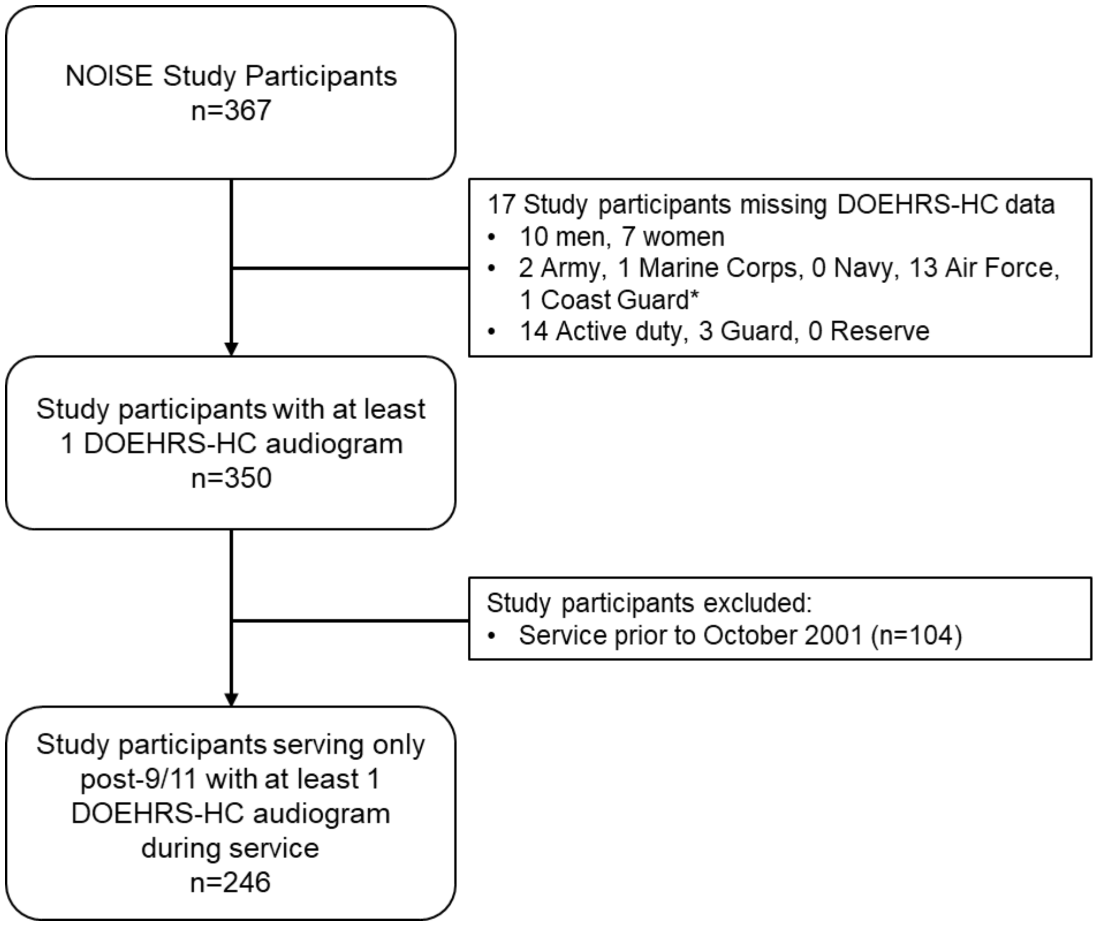
The military occupational history of study participants served as the basis for assigning a noise exposure category (defined below). Individuals were asked to note each military occupation held during service, and the timing and duration of each job held. Only military service occupations occurring within the first "continuous service period" were considered. Continuous service period is defined as having no breaks greater than one month during service. For example, if an individual had enlisted for six years, left the military, and then re-enlisted two years later, only data from the first six years of that individual's service period were used for analysis. This focused our analyses on military personnel's initial service periods because we were unable to account for noise exposures that may have occurred between service periods. For military personnel still enlisted, the end of service is defined as the date of enrollment into the NOISE Study. The study was reviewed and approved by the Institutional Review Board of the VA Portland Health Care System. Informed consent is obtained from all individuals prior to data collection, and study participants are compensated for their effort.

*DOEHRS-HC***.** In the military, audiometric surveillance is conducted using the Defense Occupational and Environmental Health Readiness System - Hearing Conservation (DOEHRS-HC).[122] The DOEHRS-HC system, which was implemented in 2000, collects, maintains, compares, and reports audiometric thresholds for DoD personnel. Currently, each branch of service (Air Force, Army, Marine Corps, Navy) and component (Active Duty, National Guard, Reserves) utilizes DOEHRS-HC to monitor the hearing health of its personnel and is an integral component of the DoD HCP. Most generally, audiometric surveillance occurs when military personnel are routinely exposed to hazardous levels of noise, just prior to and following combat deployments, and when separating from the service.

Over the time-period examined (2001-2017), the DoD HCP underwent changes. Originally cast as a risk-based conservation program, military personnel were only enrolled if they were deemed noise-exposed (i.e., at or above 85 dB A-weighted as an 8-hour time weighted average; impulse noise of ≥140 dB peak sound pressure level; or ultrasonic exposures).[84] In addition to audiometric surveillance, military personnel in the HCP are required to receive hearing protection fitting and hearing loss prevention education. In 2006, the Army began tying hearing readiness and fitness for duty to the audiogram which increased compliance with annual audiometric testing. The program was also expanded to include all Army personnel, effectively elevating the HCP to population level surveillance; the Marine Corps followed suit in 2012.[69,125] The Navy and Air Force have yet to implement these programmatic changes. Additional policies may exist between branches. As such, the total number of audiograms per individual was expected to vary based on their military service, including branch, component, occupational specialty, and whether a hearing-threshold shift was observed.

Analytic Sample. Through approved data use agreements between the VA and DoD, we received DOEHRS-HC audiograms for the first 367 NOISE Study participants enrolled at the NCRAR site. The audiograms were linked using name and social security number with NOISE Study participant data. We restricted the analysis to individuals who served only after September 2001 because this date aligns with the inception date of the DOEHRS-HC data repository (2000) and the beginning of the most recent series of military conflicts. These restrictions reduced our available sample to 246 study participants. These 246 participants provided data from 2,615 audiograms between October 2001 and June 2017, the date of data extraction. Formation of our analytic sample is displayed in Figure 4.1.

Figure 4.1. Flow chart depicting entry into the analytic sample.



4.3.2. Cumulative occupational exposure to military noise

Capturing military noise exposure information is especially challenging because military personnel work in large and acoustically diverse environments and perform a wide spectrum of operations and tasks, resulting in complex noise exposure patterns. Furthermore, quantitative dosimetry measurements are not easily accessible, which forces epidemiologic exposure assessment to be ascertained by self-report or through expert opinion. For measurable hearing-threshold change, the noise exposure has already occurred. It is thus necessary to estimate past exposures, where individual-level noise exposure was not measured. Retrospective assessment of exposures for epidemiologic purposes adds another layer of measurement complexity. Self-reported noise exposures create study validity problems to the extent that individuals with symptoms such as hearing difficulties and/or tinnitus, or knowledge of hearing loss in the absence of symptoms, may overestimate their noise exposure leading to inflated estimates of exposure-outcome relationships, a type of recall bias. Because of these inherent problems, retrospective noise exposure assessment via a job exposure matrix may be the most accurate way to reconstruct past noise exposures.

A surrogate measure of occupational noise exposure is given by a job exposure matrix (JEM) which ideally combines qualitative (e.g., service branch and occupation classification) and quantitative (e.g., workplace dosimetry) exposure information. The JEM used in the VA is the "Duty Military Occupational Specialty (MOS) Noise Exposure Listing." The VA JEM categorizes military occupations within each service branch as having a low, moderate, or high "probability of exposure to hazardous noise." The language used by the VA is "probability" and this corresponds to expert opinion alone. The JEM noise exposure rank was assigned to each military occupation held by each of the 246 study participants during their military service. Military personnel can be assigned more than one rank if they held more than one occupation. Table 4.1 highlights example military occupations and their assigned noise ranking based on the VA JEM. Using the relation between military occupation and noise exposure ranking (low, moderate, high), the number of months in a military occupation becomes a proxy measure of overall noise exposure.

Table 4.1. Example military occupations and their noise exposure ranking based on the VA job exposure matrix.

Branch of Service	Occupation Code	Occupation Description	Noise Ranking
Army	11B	Infantryman	High
Navy	78AW	Aviation Aircrewman	High
Marine Corps	08XX	Field Artillery	High
Air Force	1A0X1	Flight Engineer	High
Army	31B	Military Police	Moderate
Navy	53ND	Navy Diver	Moderate
Marine Corps	06XX	Communications	Moderate
Air Force	1C3X1	Command Post	Moderate
Army	65B	Physical Therapist	Low
Navy	28LS	Logistics Specialist	Low
Marine Corps	27XX	Linguist	Low
Air Force	1N0X1	Intelligence Applications	Low

Abbreviations: VA, Veterans Affairs

Cumulative noise exposure to an occupation was determined by each individual's audiogram date. As of each audiogram date, we computed the total number of months held in an occupation with low, moderate, and high noise exposure ranking. Basic training, which is completed by all Service members, was considered its own exposure with time exposed based on military service branch (Army = 10 weeks; Marine Corp = 13 weeks; Navy = 8 weeks; Air Force = 9 weeks).[126] At the first audiogram date, cumulative exposure is the sum of the number of months exposed to basic training. However, if no audiometric testing took place during basic training, then cumulative exposure is the sum of the number of months exposed to basic training plus the number of months exposed to an occupation between service entry and the first audiogram date. Each subsequent audiogram had the same number of months exposed as the earlier audiogram plus the number of months that occurred between audiograms. An example of how cumulative noise exposure was determined for a single individual is shown in Figure 4.2.

Figure 4.2 Example of cumulative noise exposure determination for an individual.

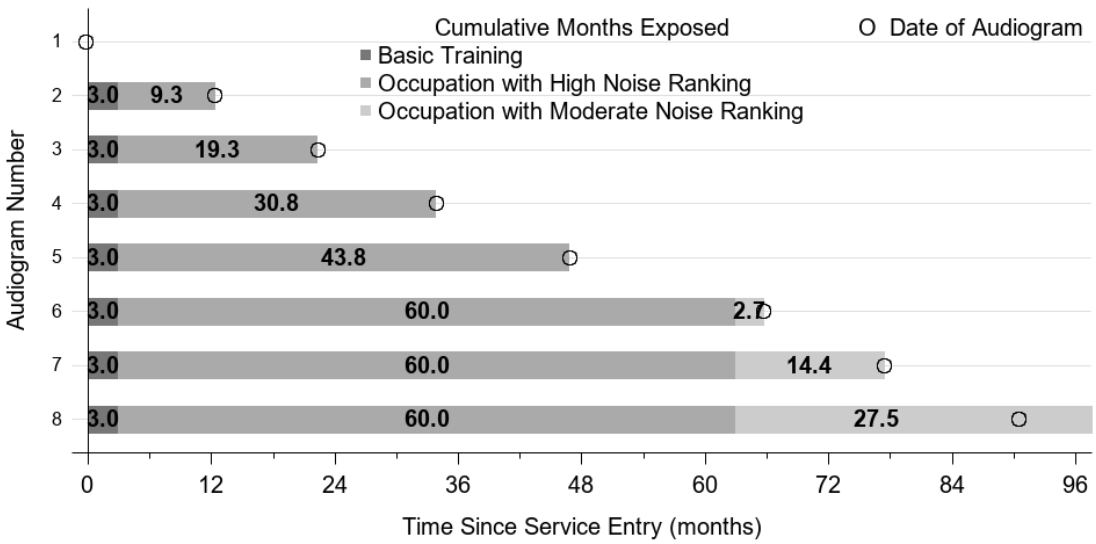


Figure legend: Each bar represents the accumulation of exposure to an occupation by the date of the audiogram. The varying shades of gray denote varying occupations. In this example, the individual was exposed to basic training noise, an occupation with a high noise ranking, and an occupation with a moderate noise ranking. Furthermore, they had an audiogram at service entry and a termination audiogram five months before separating. At the time of the separation audiogram (audiogram number 8), this individual had accumulated noise exposure during three months of basic training, 60 months at an occupation with a high noise exposure ranking, and 27.5 months at an occupation with a moderate noise exposure ranking.

The x-axis is time since service entry (in months) and the y-axis is the audiogram index, ordered from 1=first audiogram, 2=second audiogram, etc. The shaded regions of each horizontal bar represent the accumulated months of exposure to basic training (dark gray), an occupation with a high noise exposure ranking (medium gray), or an occupation with a moderate noise exposure ranking (light gray). An open circle indicates the audiogram date. In this example, the individual received an audiogram at service entry and therefore had accrued 0 months of military noise exposure. At the second audiogram, approximately 1 year after service entry, this individual had accrued 3 months of exposure to basic training and 9.3 months to a military occupation with a high noise exposure ranking. They then switched to an occupation with a moderate noise exposure ranking just before their 6th audiogram. At this time, cumulative exposure was calculated as 3 months of basic training, 60 months in a military occupation with a high noise exposure ranking, and 2.7 months in an occupation with moderate noise exposure ranking. The key point is that for each audiogram date, the effects of military occupational noise exposure are given by all the exposures up to that date.

Estimating the association between noise exposure and hearing-threshold change depends on the quality of the noise exposure assessment. The estimate can be biased if military personnel are misclassified with respect to their noise exposure status. Incorrect exposure measurements can dilute or exaggerate the relevant associations. To examine the potential for misclassification, VA JEM rankings were compared to participants' self-reported occupational noise exposure, obtained retrospectively during NOISE Study participants' baseline data collection. Study participants were asked how often they were exposed to loud noise during their occupation (response scale: never, several times a year, several times a month, several times a week, daily). Concordance between the JEM ranking and self-reported loud noise exposure was examined in tabular format using counts and proportions; this comparison is displayed in Table 4.2. There were 299 total occupations among the 246 study participants. Table 4.2 shows general concordance between the VA JEM noise rankings and self-reported noise exposure. Military personnel in occupations with a high noise exposure ranking generally reported *daily* and *weekly* exposure to loud noise, whereas personnel in occupations with low noise exposure rankings generally reported *yearly* or *monthly* exposure to loud noise. Additionally, no military personnel reported *never* having loud noise exposures. All occupations were reported to have loud noise exposures at least several times a year. The broadly similar results between the two different exposure methods increases our confidence that the noise exposure categories were accurately assigned.

Table 4.2. Self-reported frequency of exposure to loud noise by job classification noise exposure ranking[a]

Occupation Noise Exposure Ranking	Self-Reported Frequency of Loud Noise Exposure					
	Never	Several Times a Year	Several Times a Month	Several Times a Week	Daily	Total
Low	0 (0%)	22 (29.7%)	20 (27.0%)	16 (21.6%)	16 (21.6%)	74
Moderate	0 (0%)	12 (15.8%)	12 (15.8%)	24 (31.6%)	28 (36.8%)	76
High	0 (0%)	18 (12.1%)	28 (18.8%)	33 (22.2%)	70 (46.0%)	149
Total	0	52	60	73	114	299

Data displayed as n, (%)
[a] Includes 299 military occupations for 246 NOISE Study participants

4.3.3. Puretone Hearing Threshold Outcomes

The audiogram is the outcome and unit of analysis. The audiogram is composed of air-conducted hearing thresholds recorded in dB HL in both the right and left ears at six test frequencies: 500, 1000, 2000, 3000, 4000, 6000 Hz. Occasionally, an individual had repeat audiograms administered on the same day to confirm suspected hearing threshold shifts. When this occurred, only the last audiogram of the day was used. Audiograms associated with self-reported ear, nose, or throat problems were excluded from analysis (n=34 audiograms from n=15 individuals). Audiometric data were collected in a certified sound booth with equipment calibrated according to ANSI S3.1-1999 (R2003) and ANSI S3.6-2010 (R2004) standards by trained personnel (audiologists or audiometric technicians).[107] No individual had hearing threshold responses that exceeded the limits of the audiometer.

4.3.4. Covariates

Characteristics of the sample were obtained from both the DOEHRS-HC data repository and the NOISE study questionnaires administered at the time of study enrollment. Age and service branch (Army, Marine Corps, Navy, Air Force) were collected at the time of the audiogram and obtained from the DOEHRS-HC data repository; these variables were used in our statistical model (described below). To characterize our analytic sample, we used age and service branch information obtained at the time of enrollment in the NOISE Study. Sex (male/female), race/ethnicity (white/other than white), enlistment duration, service component (Active, Reserve, National Guard), number of deployments (0, 1, 2, 3 or more), and number of military occupations were also derived from the NOISE Study.

4.3.5. Statistical Analysis

The overall goal of analysis was to estimate the average annual rate of hearing-threshold change during military service among post-9/11 Veterans by military occupational noise exposure ranking. Pure-tone thresholds are expected to naturally vary among individuals, between ears within the same individual, and across frequencies within ears of the same individual. We estimated the average annual rate of hearing-threshold change using results of a hierarchical linear model (HLM), accounting for the natural variability in pure-tone thresholds. Additionally, this analytic approach accounts for unequal intervals and missing observations.[127] Thus, all observations (including military personnel with only one audiogram) are retained in the analysis, contributing to the estimation of regression parameters at the time for which participants contributed data.

We modeled the cumulative probability of noise exposure based on military occupation (in months) and frequency as an interaction term and fit our regression model with both frequency and frequency-squared (frequency^2) terms. The model also included age at the time of the audiogram. Two-way interactions between age and frequency, and between age and frequency^2 were included to allow frequency changes to vary by age. Service branch at the time of the audiometric visit was included; three-way interactions among service branch, frequency, and frequency^2, and cumulative noise exposure were included to allow the longitudinal patterns of change to vary with service branch and to allow the rates of changes in threshold to vary with different occupations and frequencies. Finally, to account for natural variation in the rates of change, subject-specific frequency effects along with a subject-ear random intercept were included. To summarize, the final model contained 70 fixed effects (age, frequency, frequency^2, service branch, cumulative noise exposure by military occupation, and interaction terms defined above) and two random effects (subject-specific frequency and subject-ear). Further details of the statistical approach are provided in Appendix C.

Our aim was to estimate the average annual rate of pure-tone hearing threshold change as a consequence of accumulated exposure to military occupational noise. To do this, we modeled the effects of cumulative exposure to a military occupation on the average pure-tone threshold, so that the average change with one year of exposure to a military occupation is the difference between the model-based average pure-tone threshold with one year of exposure to a military occupation minus the model-based average threshold with no exposure. We estimated the 95% confidence intervals (CI) around the estimates of the average annual hearing-threshold change. A 95% CI that includes zero is consistent with the null hypothesis of no pure-tone hearing-threshold change.

4.4. Results

Among the 246 study participants, most were men (87%), non-Hispanic white (68%), and young (median age 20 years at the time of enlistment, Table 4.3). Additionally, over half of the analytic sample were in the Army (58%). The median duration of enlistment was six years and most, during that time, had one military occupational classification (82%). The median number of audiograms across 246 study participants was 5 (range 1-17). Seven individuals had only one audiogram, while 11 had 10 or more audiograms (Appendix, Table C.1). The total number of audiograms varied by service branch and year (Appendix, Table C.2). Median number of audiograms among Army, Navy, Marine Corps, and Air Force Service members were 6 (range 2-17), 4 (range 2-14), 4 (range 1-10), and 4 (range 1-15), respectively.

Table 4.3. Participant-level characteristics of analytic sample

Characteristic	n=246
Gender, n (%)	
Male	214 (87%)
Female	32 (13%)
Age at Service Entry, years (median, range)	20 (17-40)
Race/Ethnicity, n (%)	
Non-Hispanic White	168 (68%)
All Other Races/Ethnicities	72 (29%)
Declined to Report/Missing	6 (2%)
Enlistment Duration, years (median, range)	6.0 (1.5-15)
Branch of Service, n (%)	
Army	142 (58%)
Marine Corps	50 (20%)
Navy	35 (14%)
Air Force	19 (8%)
Service Component, n (%)	
Active	204 (83%)
National Guard	28 (11%)
Reserves	14 (6%)
Number of deployments, n (%)	
0	23 (9%)
1	144 (59%)
2	40 (16%)
3 or more	39 (16%)
Number of military occupations, n (%)	
1	202 (82%)
2	36 (15%)
3 or more	8 (3%)
Number of audiograms, median (range)	5 (1-17)

Pure-tone thresholds corresponding with first and last audiograms for our sample are shown in Figure 4.3, left and right panels respectively. Audiometric thresholds by frequency for each individual's ear (in gray) and the group average of threshold by frequency (in black) across individuals is displayed. On average, hearing 500-6000 Hz was audiometrically normal at the first encounter, although some individuals did have hearing loss at the first audiogram. The last audiogram occurred, on average, 5.3 years after the first audiogram (range: 0.5-14 years). At the last audiogram, the group average was slightly poorer across all test frequencies when compared to the first audiogram and remained within normal range (≤20 dB HL). However, the beginning of a noise notch was observed in the group average at the last audiogram. Individually, 28% of our sample (69/246) had at least one pure-tone response with a threshold that was >20 dB HL, suggesting at least a mild hearing loss for one ear. By the last audiogram, 46% of our sample (110/239) had at least one pure-tone response that exceeded 20 dB HL. This suggests a 64% increase in the prevalence of audiometric hearing loss between the first and last audiogram.

Figure 4.3. Spaghetti plots of audiometric thresholds

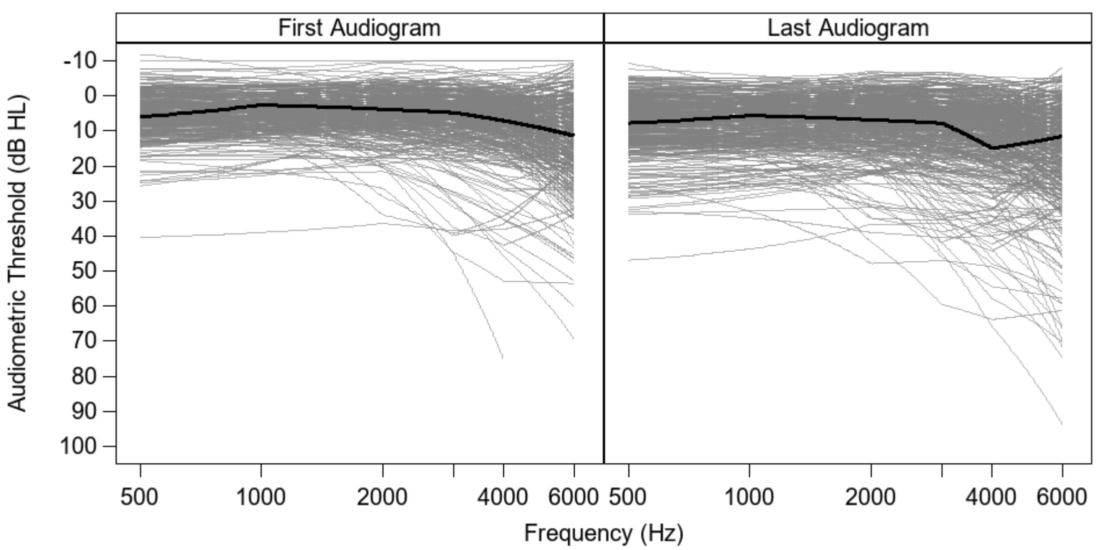


Figure legend: Thresholds are plotted by frequency for each individual's ear (in gray) and the group average of threshold by frequency (in black) across individuals, at the first and last visit.

4.4.1. Rate of Change

Figure 4.4 shows the estimated average annual rate of hearing-threshold change by audiometric test frequency for 500-6000 Hz for each service branch; positive values suggest hearing degraded and negative values suggesting hearing improved. Average annual rates of hearing-threshold change are plotted by military occupational noise exposure rank and varied between -0.5 dB per year of exposure to 1.1 dB per year of exposure. The data along the x-axis within each panel reports the estimated average hearing-threshold change in dB/year of exposure for each service branch by test frequency. There were too few Air Force Service members in occupations with low or moderate noise exposure ranking to provide stable estimates of the average annual rate of hearing-threshold change.

A linear dose-response pattern in which increasing noise exposure ranking is associated with increasing hearing-threshold change did not emerge. However, some patterns within service branches are notable. Among Marine Corps personnel, the annual rate of hearing-threshold change was the greatest for individuals with military occupations with a high noise exposure ranking. For 2000–6000 Hz, the average annual rate of hearing-threshold change increased from 0.6 to 1.1 dB per year. In the Army, the average annual rate of hearing-threshold change was the greatest among personnel with exposure to a military occupation with a moderate noise exposure ranking. On average, Army personnel experienced hearing-threshold change from 0.3 to 0.6 dB per year from 3000-6000 Hz. Additionally, Army personnel with a high noise exposure ranking demonstrated elevated hearing-threshold changes at 500 Hz (0.4 dB per year). Navy personnel with a high noise exposure ranking demonstrated a threshold change of -0.5 dB per year at 2000 Hz, an improvement in thresholds over time. No statistically significant hearing-threshold changes were observed among Air Force study participants.

Figure 4.4. Average annual rate of hearing-threshold changes

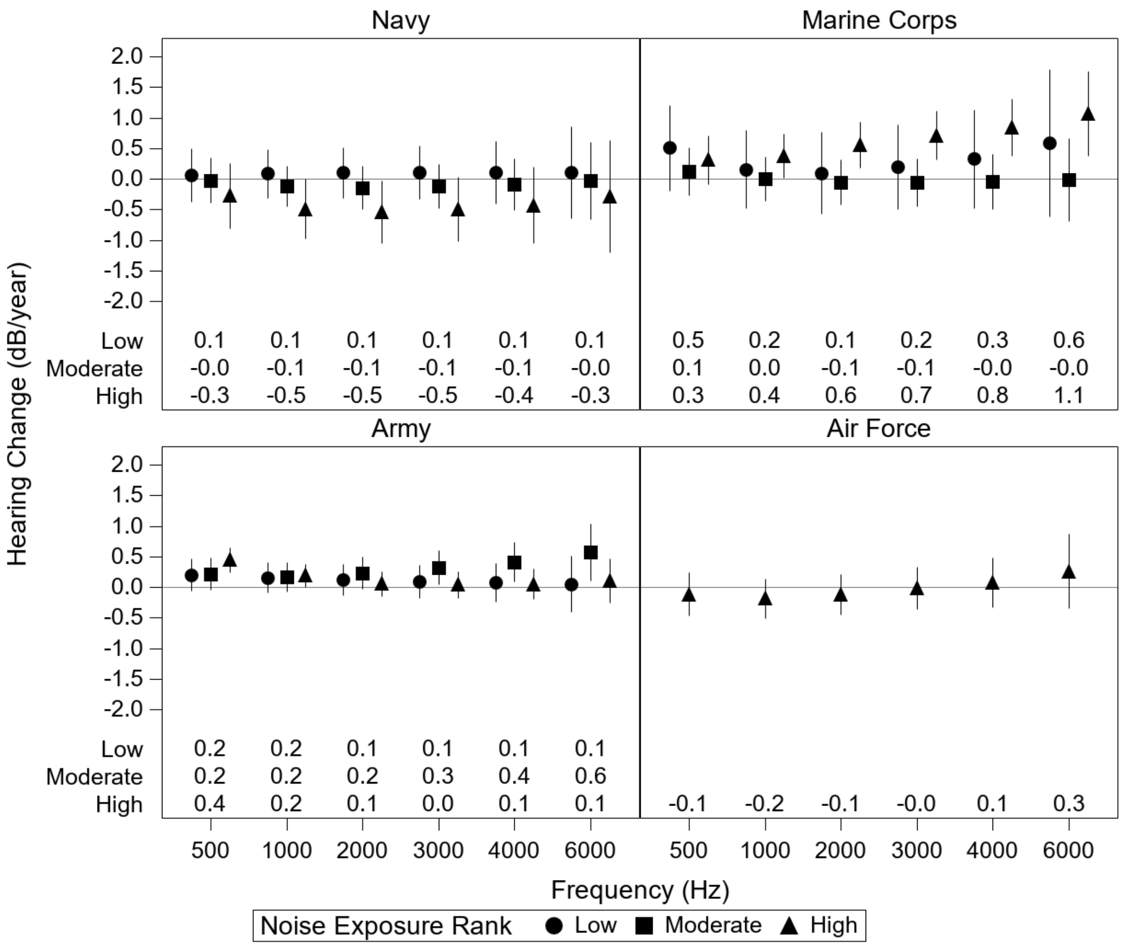


Figure legend: Data are plotted by audiometric test frequency for each service branch and occupational noise exposure ranking. Corresponding hearing change value shown in the table within each panel.

4.5. Discussion

This analysis describes the longitudinal progression of hearing-threshold change for 246 individuals enrolled in the NOISE Study using audiometric data extracted from the

DOEHRS-HC data repository. Joining the NOISE Study data with the DOEHRS-HC data provided an opportunity to examine associations between military occupational noise exposure and hearing over time during service. The average annual rate of hearing-threshold change varied by service branch, military occupational noise exposure ranking (low, moderate, and high), and audiometric frequency. Determining the rate of hearing-threshold change and potential risk factors that affect the rate of change is important to elucidate the impact of military service on hearing and to guide prevention strategies and subsequent care. To our knowledge, this unique application of DOEHRS-HC data is the first analysis of hearing-threshold change over time and contributes to the limited literature on longitudinal effects.

We estimated that the average rate of hearing-threshold change varied between -0.5 to 1.1 dB per year when stratified by service branch, military noise exposure ranking, and audiometric-test frequency. Generally, the higher test frequencies demonstrated the greatest average annual rates of hearing-threshold change consistent with noise exposure. However, linear dose-response associations were not observed. Army occupations with a moderate noise ranking, and Marine Corps occupations with a high noise ranking, demonstrated the highest average rates of hearing-threshold change – the latter more so than the former. On average, Navy and Air Force personnel did not display meaningful hearing-threshold changes; the exception being Navy personnel with a high noise exposure rank demonstrating an improvement at 2000 Hz. The difference in hearing-threshold degradations across the military branches is likely indicative of the varying types of noise these branches are exposed to and, importantly, varying policies on hearing protection device use and enforcement.[125] The observed improvement in hearing thresholds over time among Navy personnel was an unexpected finding. Further longitudinal research examining hearing among this service branch is warranted.

No longitudinal study of military personnel currently reports the average annual rate of hearing-threshold change by frequency for comparison. One longitudinal study with Veterans is available for comparison: The VA Normative Aging Study.[128] In this study, Veterans aged 21-81 were followed from 1962-1996 and their average annual rate of change was reported by frequency and age group. The average rate of hearing-threshold change in the 30-39 year age group (the closest age group to our study that was reported) ranged from about 0.1 dB/year to just under 0.7 dB/year for frequencies 500-6000 Hz.[128] Generally, our estimates of hearing-threshold change across frequencies, service branches, and military occupational noise exposure rankings were less than what was reported by The VA Normative Aging Study. Since the end of the audiometric assessment of the VA Normative Aging Study, concerted efforts have attempted to improve the DoD HCP. The difference between the VA Normative Aging Study and our estimates of the average annual rate of hearing-threshold change could be the product of improved hearing conservation efforts between study periods. However, despite potential improvements in hearing conservation, the estimated average annual rates of hearing-threshold change among Marine Corps personnel exposed to military occupations with a high noise exposure ranking enrolled in the NOISE Study exceeded the published estimates of the 30-39 year old group from the Normative Aging Study. Our estimates of annual change are most closely aligned with those among Veterans aged 50-59 in The

VA Normative Aging Study. This suggests that the hearing thresholds of Marine Corps personnel in an occupation with a high noise exposure ranking is declining at a faster rate than what would be expected for their age group.

The lack of a dose-response may not be surprising when considering hearing-threshold changes in the presence of hearing protection device use. A report by the Government Accountability Office[125] noted that inconsistencies in various military strategies for hearing protection and the lack of adequate surveillance and oversight placed military personnel unnecessarily at risk for hearing loss. Since 2006, the Army has made concerted efforts to enroll all of their military personnel into the HCP, which includes annual audiometric surveillance and hearing protection device fitting. Thus, Army personnel exposed to occupations with a moderate noise ranking are being surveilled and fit with hearing protection who otherwise might not have been tested in an HCP based solely on high noise dosimetry measures (i.e., ≥85 dBA).

Service members who are exposed to moderate amounts of noise may feel that hearing protection devices provide excessive attenuation, leading to a decrease in their ability to communicate and perform job duties. Thus, compliance with hearing protection may vary based on noise exposure and, at moderate noise levels, hearing protection use may not be enforced. This patterned outcome may be expressed in the population level surveillance currently used by the Army. At least one study of a non-military, industrial occupational cohort indicated the lack of a dose response was likely related to varying hearing protection use among the different occupational noise levels and noted that hearing protection use may not be required or enforced by management at moderate levels.[129] By comparison, those in occupations with high noise exposure rankings may find that use of hearing protection results in less fatigue, pain, tinnitus, and hearing-threshold shifts and thus may be more compliant and consistent with hearing protection use. This suggests hearing protection fitting strategies may need to be altered to provide adequate protection without excessive attenuation and that continued efforts should be made to improve on-site earplug selection, fit-testing, and training in the use of individually fitted protection.

Our results must be interpreted against the backdrop of changing HCPs and auditory surveillance strategies by service branches. During the time period examined (2001-2017), the vast majority (>90%, Appendix Table C.2) of Army audiograms occurred after 2006 when the Army began tying audiometric surveillance to fitness for duty and expanded enrollment to include all Army personnel. Thus, the Army results are more likely to represent population-level hearing health behaviors and hearing-threshold changes over time compared to the other service branches. While the Marine Corps launched their population-level audiometric surveillance in 2012, many audiograms examined in this study were collected prior to this policy change (67%, Appendix Table C.2). Consequently, the results from the Marine Corps are likely reflecting more of the risk-based auditory monitoring strategy employed by the Armed Services for many years. Differing surveillance/monitoring strategies thus reflect different populations of interest and may highlight differences in exposure and hearing protection use patterns, helping explain the lack of a dose-response association.

4.5.1. Strengths, Limitations, and Future Directions

This study has several strengths. First, the study used repeat audiograms over time and the retrospective assignment of noise exposure rankings to aid in our understanding of the impacts of occupational noise on hearing during military service. Second, in analyzing the rate of hearing-threshold change by frequency, we have expanded our understanding of how slowly or rapidly hearing deteriorates at a population-level and within different service branches. Therefore, a deeper understanding of the time course and rate of hearing-threshold changes, and the factors that influence hearing-threshold changes, will aid the DoD in designing more effective hearing-loss prevention interventions. Finally, the hierarchical linear modeling approach allowed us to utilize all available data.

Our study is not without limitations. The main limitation with job exposure matrices is that specific risk factors cannot be clearly identified. For example, Service members are exposed to noise, but they may also be exposed to solvents, inhalants, medications, and other stressors in the workplace. Additionally, if only some personnel within a military occupation are exposed to noise while others are not, the heterogeneity within the group may mask the ability to observe associations between noise and hearing. With these limitations in mind, an observed elevated risk in hearing-threshold change in a military occupation only suggests risks from noise exposure and more precise etiologic questions relating to hearing outcomes remain. Taken together, our study results may not be generalizable to the entire Armed Services.

In the future, attention should be given to the development of a more robust military job exposure matrix that adjusts for hearing protection use and incorporates noise dosimetry measures when available. This would strengthen the ability to epidemiologically assess the association between military occupational noise and hearing, which would be instrumental to uncovering how early noise exposures, including noise exposures that induce permanent hearing shifts but remain within the normal range, as well as hearing loss, impact hearing later in life. Moreover, future work should include a larger and more diverse group of military personnel, including military personnel low noise exposures.

4.5.2. Conclusion

This study used the audiometric data of military personnel collected as part of the DoD HCP to determine the average change in audiometric thresholds by frequency over time and estimated how military occupational noise exposure altered that trajectory. This was, to our knowledge, the first analysis of hearing-threshold changes over time using such data and adds to the limited literature on frequency-specific hearing outcomes during military service. Based on this analysis, we estimate that some military personnel are at increased risk for hearing-threshold changes due to occupational noise exposure and hearing sensitivity may be declining at faster rates than would be expected for their age group. Estimates of the amount of hearing-threshold change by frequency, and risk factors that impact hearing inform DoD efforts to protect Service members' hearing during their military service.

Chapter 5. Blast Exposure and Self-reported Hearing Difficulty in Normal Hearing Service Members and Veterans: The Mediating Role of Post-traumatic Stress Disorder

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Author Contributions: All authors contributed to this work. Dr. Henry and Dr. Carlson designed the principal study and reviewed the data. Drs. Snowden and Gallun provided expert opinion and interpretive analysis. Kelly Reavis designed the study's analytic strategy, analyzed the data, and wrote the main paper. All authors discussed the results and implications and commented on the manuscript at all stages.

5.1. Abstract

Evidence suggests military blast exposure may lead to self-reported hearing difficulties despite audiometrically normal hearing, yet research identifying potential mechanisms of this association remains limited. PTSD may mediate the effects of blast on self-reported hearing difficulty among individuals with normal hearing through psychological and attentional changes that alter symptom perception. Baseline data from the Noise Outcomes in Servicemembers Epidemiology Study (2014-2019) were used to test this hypothesis (n=477 enrolled in Portland, Oregon and San Antonio, Texas). Using regression models and following a formal causal mediation framework, we estimated total associations, natural direct and indirect associations, and percent mediated. We found that individuals with blast exposure had higher prevalence of probable PTSD, and a higher prevalence of self-reported hearing difficulty, than individuals without blast exposure. Compared to participants without blast exposure, those with blast exposure had twice the prevalence of self-reported hearing difficulty (prevalence proportion ratio=2.0, 95% confidence interval: 1.3-3.0), with 41% of the association mediated through probable PTSD. This information should inform the assessment and care coordination for Service members and Veterans who express difficulty hearing but have audiometrically intact hearing.

5.2. Introduction

Blast exposure is a known risk factor for hearing loss, especially in the military population.[10-13,51] Increased insurgence warfare in post-9/11 wars has led to an increase in blast exposures among military Service members compared to past wars.[51] Thanks to advanced personal protective equipment and combat casualty care capabilities, today's Service members are more likely to survive blast-related injuries. This progress means that more Service members return home alive, but many suffer with lasting deficits and disabilities.[51,59] The ear is particularly vulnerable to a blast pressure wave because it is the body's most sensitive pressure transducer.[12,13] In a sample of deployed male Service members, Joseph and colleagues[11] found that individuals with a blast-related injury were twice as likely to have peripheral hearing loss compared to individuals with a non-blast related injury (OR=2.2; 95% CI: 1.4-3.4) and attributed 49% of the risk to the blast event. Although individuals with peripheral hearing loss are likely to report increased difficulty understanding speech in noise and in other complex acoustic environments, complaints of hearing difficulty with normal or near-normal hearing are a separate hearing health challenge and have also been reported.[14,15,62,130]

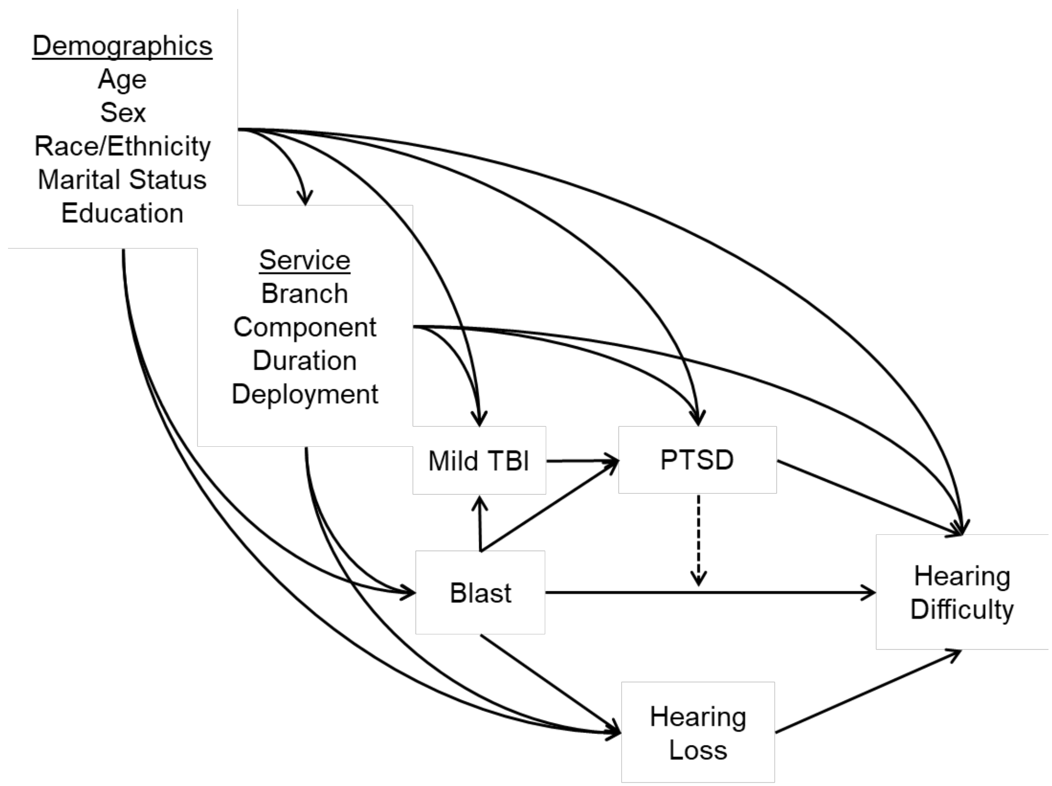
Veterans whose hearing tests show normal or near-normal peripheral hearing have reported hearing difficulties when trying to understand the content of speech in the presence of noise, when attempting to follow long conversations, and when listening by telephone.[14] Among blast-exposed Veterans with normal to near-normal hearing, 60% self-reported difficulty hearing compared to only 7% without blast exposure.[62] Central auditory nervous system pathways and cognitive processes are necessary to support communication in complex listening environments. Understanding speech and conversation in noise requires perceptual separation and/or integration of sounds.[15] One theorized mechanism of blast-related hearing injury describes the blast wave propagating through the brain, resulting in contusions, shearing, and diffuse axonal injury within central auditory structures.[16,63] While earplugs and helmets may offer some degree of protection from blast-related peripheral hearing and head injury, these measures do not effectively protect the central auditory nervous system from blast wave effects. Resulting damage may be responsible for hearing difficulties among those who have normal peripheral hearing.

The ability to understand speech in noise and in other complex acoustic environments also requires sustained attention and focus on the target speech signal. This involves cognitive functions that remain mostly outside auditory structures. Two pathologies that are not specific to the auditory system and may interfere with sustained attention and focus are traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD).[93,94] TBI is often categorized as mild (also referred to as "concussion"), moderate, or severe. Approximately 80% of all military TBIs are categorized as mild.[51,86] Evidence connecting mild TBI to TBI-related symptoms and sequelae is inconsistent and is often attributable to PTSD symptoms.[131,132] It is not surprising then that these two pathologies frequently co-occur; 64%-73% of Iraq and Afghanistan war Veterans with a diagnosis of mild TBI also have a co-morbid PTSD diagnosis.[89,90] The most common cause of TBI among U.S. forces deployed to Iraq and Afghanistan is blast exposure, which can also result in PTSD.[51] For these reasons, and because PTSD symptoms are potentially modifiable, it is important to recognize and assess PTSD as a possible mediator of sensory sequalae linked to blast exposure.

Individuals with PTSD often describe difficulties with concentration, attention, and memory.[94,133] Veterans with PTSD have shown deficits on tasks that require working memory, sustained attention, and processing speed.[93,133] One conceptual framework suggests that poor health outcomes in PTSD may be linked to psychological and attentional changes that alter symptom perception.[99] Considering the well-established relationship between military blast exposure and PTSD,[51] it is possible that effects of blast on hearing difficulty may also be mediated by PTSD. The role of PTSD has not been previously studied as a possible mediator between blast exposure and hearing sequelae. Relevant studies have only expressed the high co-occurrence of blast exposure and PTSD, noting the marked complexity in understanding the contributions of PTSD to the observed association.[14,15,61,62,130] This points to the need for a unifying conceptual framework for blast-related functional hearing difficulties that integrates PTSD.

The primary aim of this study was to examine, in a group of Service members and Veterans, the associations between blast, PTSD, and self-reported hearing difficulty, and secondarily, to examine PTSD as a possible mediator of the association between blast exposure and hearing difficulty. An improved understanding of mechanisms that mediate an association imparts support of the primary association while also highlighting a new potential target for intervention. We build upon past examinations by proposing an a priori causal relationship between blast, PTSD, and self-reported hearing difficulty as depicted in our conceptual model (Figure 5.1). The conceptual model highlights five epidemiologic questions that motivated our study – What is: (1) the effect of blast on PTSD? (2) the effect of PTSD on self-reported hearing difficulty? (3) the total effect of blast on self-reported hearing difficulty? (4) the direct effect of blast on self-reported hearing difficulty (i.e., the effect not mediated through PTSD)? and (5) the indirect effect of blast on self-reported hearing difficulty mediated through PTSD?

Figure 5.1 Modified causal diagram



Abbreviations: TBI, traumatic brain injury; PTSD, post-traumatic stress disorder
Figure legend: Solid arrows depict potential causal pathways. Dashed arrow suggests potential effect measure modification of a causal path.

5.3. Methods

The Noise Outcomes In Servicemembers Epidemiology Study ("NOISE Study") was designed to examine longitudinal effects of military and non-military exposures on auditory functioning among post-9/11 Service members and Veterans.[106] Study recruitment and follow-up are ongoing. The sample includes active duty Service members and Veterans who have recently (within ~2.5 years) separated from the military. Participants in this study have been enrolled at the Veterans Health Administration (VA) National Center for Rehabilitative Auditory Research, located at the VA Portland Health Care System in Portland, Oregon and at the Department of Defense Hearing Center of Excellence on Joint Base San Antonio, in San Antonio, Texas. Potential study participants were excluded if they did not serve in a post-9/11 conflict or if they have been separated for more than 2.5 years from military service. Study participants undergo a comprehensive hearing test and complete surveys to capture demographics, military service history, including exposure to blast, and health conditions such as symptoms of PTSD.

Using cross-sectional baseline data, the analytic cohort for this study was limited to study participants enrolled between 2014-2019 with normal hearing defined as hearing thresholds ≤20 decibels hearing level (dB HL) from 250-8000 Hz. We excluded individuals with a history of moderate or severe TBI from our analysis. Moderate to severe TBI likely yields a different conceptual model than presented in Figure 5.1. Informed consent was obtained from participants prior to data collection, and they were compensated for their effort.

5.3.1. Exposure Measurement: Blast

The Traumatic Brain Injury and Blast Exposure History Questionnaire was designed specifically for our study to assess participant history of probable TBI and blast exposures. This questionnaire was adapted from the Comprehensive TBI Evaluation used clinically by the VA.[134] To capture information about blast exposure, participants were asked: "Now we are going to ask you about your blast exposures, whether or not you experienced any injuries related to blasts. When a high explosive bomb or improvised explosive device (IED) goes off, there is a 'blast wave,' which is a wave of highly compressed gas that hits solid objects like a person's body and may feel almost like smashing into a wall. Do you remember experiencing this type of 'blast wave' or ever being told that you experienced it?" Response options are 'yes', 'not sure', or 'no'. For the current analysis, blast exposure was coded dichotomously (yes/no) with all responses of 'unsure' recoded as 'no.'

5.3.2. Mediator Measurement: PTSD

PTSD was measured using the Primary Care-PTSD-4 screening questionnaire.[135] The PTSD-4 is a four-item questionnaire used in primary care and other clinical settings at the VA. The screening questionnaire begins with a sentence to cue study participants to consider traumatic events. Participants noting a traumatic event are asked if that event was so upsetting that over the last month they: (1) had nightmares about the event; (2) avoided situations that reminded them of the event; (3) were "on guard"; or (4) felt detached from others and their surroundings. If responses were 'yes' to at least three items, participants were considered to have probable PTSD. The PTSD-4 has been shown to have high sensitivity (0.78) and specificity (0.87) when compared to a PTSD diagnosis in a Veteran primary care population.[135]

5.3.3. Outcome Measurement: Self-reported Hearing Difficulty

Self-reported hearing difficulty was captured using the Hearing Handicap Inventory for Adults (HHIA).[136] The HHIA is a 25-item questionnaire designed to measure the emotional and social adjustment of people with perceived hearing difficulty. It is appropriate to administer regardless of whether peripheral hearing loss is present. Responses to the items include 'yes' (4 points), 'sometimes' (2 points), and 'no' (0 points). Scores range from 0 to 100, with higher scores indicating greater hearing difficulties. The HHIA was coded dichotomously without differentiation between social and emotional impacts; total scores 0-16 suggest no difficulty and scores >16 suggest the presence of functional hearing difficulty.[136]

5.3.4. Covariates

Potential confounders were selected *a priori* using directed acyclic graphs (DAGs); these were informed by theory and prior knowledge (Appendix Figure D.1).[137,138] All potential confounders were self-reported and included: sex (Male; Female), age (in years), race (White; African American/Black; American Indian/Alaskan Native; Asian; Hawaiian/Pacific Islander; Other or Selected >1 Race; Prefer Not To Answer/Missing), ethnicity (non-Spanish/Hispanic/Latino; Spanish/Hispanic/Latino), marital status (Living with Spouse/Partner; Single/Never Married; Divorced/Separated/Widowed), education (Some/Completed High School; Some College Vocational; Completed College), service branch (Army; Marine Corps; Navy/Coast Guard; Air Force), duration of service (in years), and deployment to a conflict zone (Yes; No). In the analysis of effects of PTSD on hearing difficulty, blast exposure was also included as a potential confounder. If a Service member or Veteran had enlisted in more than one service branch, then service branch was assigned based on longest duration of service.

5.3.5. Statistical Analysis

Our sample consisted of 490 Service members and Veterans with normal hearing. Thirteen participants (2.7%) had one or more missing variables and were excluded from the analysis (final n=477). Mediation terminology used is total effects, natural direct effects (NDE), natural indirect effects (NIE), controlled direct effect (CDE), and pure indirect effects (PIE); however, because this is a cross-sectional analysis of baseline data, we use the term "association" rather than "effect" to describe the results. All analyses were conducted using SAS software, version 9.4.

Unadjusted and adjusted total effects analysis. Covariate distribution was examined among study participants with and without blast (exposure) as well as with and without probable PTSD (mediator). Bivariable and multivariable log-binomial models were used to first estimate prevalence proportion ratios (PPR) and 95% confidence intervals (CI) describing the association between blast exposure and self-reported hearing difficulty and between blast exposure and probable PTSD. Next, bivariable and multivariable log-binomial models were used to estimate PPR and 95% CI describing the association between probable PTSD and self-reported hearing difficulty, including adjustment for blast exposure (a confounder of the PTSD/ self-reported hearing difficulty association).

Unadjusted models and models adjusted for demographic and service characteristics are presented. Due to small cell sizes, race and ethnicity were collapsed into a single variable reflecting non-Hispanic White study participants versus all other races/ethnicities for inclusion in the adjusted models. We conceptualized this covariate as an indicator of discrimination and racism rather than as a biologic risk factor, given racism likely structures adverse military exposures and health outcomes.[139] We assessed the sensitivity of our adjusted regression models to potential unmeasured confounding by computing an e-value; the e-value is an estimation of strength of association between an unmeasured confounder and exposure, as well as outcome, necessary to suggest a reasonable alternative explanation for the observed association.[140]

Mediation analysis, accounting for exposure/mediator interaction. The secondary aim was to partition the total effect between blast exposure and self-reported hearing difficulty into direct and indirect effects; accordingly, natural effects were estimated as opposed to controlled effects, given that controlled indirect effects are irresolvable.[141,142] We used mediation analysis methods based on a regression framework for a common dichotomous outcome.[143,144] The NDE and NIE of the blast-hearing difficulty relationship were estimated by fitting a log-binomial model for self-reported hearing difficulty (Y), conditional on blast exposure (A), probable PTSD (M), a blast-PTSD interaction variables (AxM), and a set of confounders (C): $log\{P(Y = 1|A = a, M = m, C = c)\} = \theta_0 + \theta_1 a + \theta_2 m + \theta_3 am + \theta_4' c$ as well as a logit model for probable PTSD, conditional on blast exposure and confounders: $logit\{P(M = 1|A = a, C = c)\} = \beta_0 + \beta_1 a + \beta_2' c$.[145] The proportion of the increased blast exposure, self-reported hearing difficulty association that is mediated (i.e., proportion mediated) through probable PTSD was computed on the prevalence proportion difference scale as $Hearing\ Difficulty\ \% = [PPR_{NDE} \cdot (PPR_{NIE} - 1)/(PPR_{NDE} \cdot PPR_{NIE} - 1)] \cdot 100$ [143]. Four-way decomposition was used to disentangle the association between blast exposure and hearing difficulty by probable PTSD, explaining 'how' and 'for whom' a cause affects an outcome.[146] Four-way decomposition includes estimating the following effects: the CDE, reference interaction, mediated interaction, and the PIE. Standard errors were obtained using the delta method. E-values were estimated for our causal mediation analysis to examine the potential impact of an unmeasured confounder on our results.[140]

5.4. Results

Of the 477 Service members and Veterans with normal peripheral hearing, 113 (23.7%) reported blast exposure, 109 (22.9%) screened positive for probable PTSD, and 100 (21.0%) reported hearing difficulty, according to the HHIA. Forty-nine (10.3%) participants reported having blast exposure and screened positive for probable PTSD. The median level of self-reported hearing difficulty was 4 (HHIA range: 0-96). Baseline characteristics of the study sample by blast history (exposure) and probable PTSD (mediator) are shown in Table 1. The average age in the sample was about 31 years and varied little by blast exposure or by probable PTSD. Blast exposure and probable PTSD was experienced by more male than female participants and more by participants reporting combat deployment than those without combat deployment (Table 5.1). Hearing was within normal limits across frequencies for the sample and there were no observable differences in mean hearing thresholds between those with and without blast exposure or with and without probable PTSD.

Table 5.1. Distribution of covariates by blast (exposure) and probable PTSD (mediator)

Characteristic	Blast Exposure		Probable PTSD		Total
	Yes (n=113)	No (n=364)	Yes (n=109)	No (n=368)	
	n (%)	n (%)	n (%)	n (%)	n
Sex					
Male	98 (29.8)	231 (70.2)	82 (24.9)	247 (75.1)	329
Female	15 (10.1)	133 (89.9)	27 (18.2)	121 (81.8)	148
Age years; mean (SD)	32 (6.9)	31 (7.3)	31 (6.9)	31 (7.3)	477
Hearing 0.25-3 kHz Average					
Right ear; mean (SD)	9.9 (4.2)	8.4 (3.8)	9.9 (3.9)	8.4 (3.9)	477
Left ear; mean (SD)	9.8 (4.6)	8.3 (4.0)	10.1 (4.2)	8.2 (4.1)	477
Hearing 4-8 kHz Average					
Right ear; mean (SD)	8.3 (4.5)	6.4 (4.2)	7.8 (4.1)	6.6 (4.4)	477
Left ear; mean (SD)	8.0 (4.6)	6.3 (4.3)	7.7 (4.1)	6.4 (4.5)	477
Race/Ethnicity					
Non-Hispanic White	70 (24.4)	217 (75.6)	67 (23.3)	220 (76.7)	287
All other Races/Ethnicities	43 (22.6)	147 (77.4)	42 (22.1)	148 (77.9)	190
Marital Status					
Living with Spouse/Partner	70 (26.1)	198 (73.9)	63 (23.5)	205 (76.5)	268
Single, Never Married	24 (16.1)	125 (83.9)	32 (21.5)	117 (78.5)	149
Divorced/Separated/Widowed	19 (31.7)	41 (68.3)	14 (23.3)	46 (76.7)	60
Education					
Some/Completed High School	10 (21.7)	36 (78.3)	13 (28.3)	33 (71.7)	46
Some College/Vocational	71 (26.4)	198 (73.6)	72 (26.8)	197 (73.2)	269
Completed College	32 (19.8)	130 (80.2)	24 (14.8)	138 (85.2)	162
Military Branch					
Army	62 (40.5)	91 (59.5)	48 (31.4)	105 (68.6)	153
Marine Corps	19 (33.9)	37 (66.1)	21 (37.5)	35 (62.5)	56
Navy/Coast Guard	9 (13.4)	58 (86.6)	17 (25.4)	50 (74.6)	67
Air Force	23 (11.4)	178 (88.6)	23 (11.4)	178 (88.6)	201

Military Component									
Active	90	(21.4)	331	(78.6)	92	(21.9)	329	(78.1)	421
National Guard/Reserve	23	(41.1)	33	(58.9)	17	(30.4)	39	(69.6)	56
Duration years; median (range)	8.0 (2-28)		6.6 (0.2-31)		7.2 (1.5-28)		7.0 (0.2-31)		477
Combat Deployment									
Yes	106	(35.8)	190	(64.2)	88	(29.7)	208	(70.3)	296
No	7	(3.9)	174	(96.1)	21	(11.6)	160	(88.4)	181
Probable History of Mild TBI									
Yes	39	(68.4)	18	(31.6)	22	(38.6)	35	(61.4)	57
No	74	(17.6)	346	(82.4)	87	(20.7)	333	(79.3)	420

Abbreviations: PTSD, post-traumatic stress disorder; SD, standard deviation; kHz, kilohertz; TBI, traumatic brain injury.
N (%) are displayed unless otherwise noted. Row percentages are shown.

5.4.1. Total Effects Analysis

Prevalence proportion (%), unadjusted and adjusted PPR, and the 95% CI of the observed associations are presented in Table 5.2. Participants with blast exposure had a higher prevalence of self-reported hearing difficulty, and a higher prevalence of probable PTSD, compared to those without blast exposure. After adjusting for potential confounders, those with blast exposure had 2.0-fold (95% CI: 1.3, 3.0) higher prevalence of self-reported hearing difficulty (Table 5.2A, Model 3) and 1.8-fold (95%: 1.3, 2.6) higher prevalence of probable PTSD (Table 5.2B, Model 3), compared to those without blast exposure.

Additionally, 49% of participants with probable PTSD versus 13% of those without probable PTSD reported difficulty hearing. After adjusting for potential confounders, including blast exposure, those with probable PTSD had 3.1-fold (95% CI: 2.2, 4.3) higher prevalence of self-reported hearing difficulty than those without probable PTSD (Table 5.2C, Model 3). Further adjustment for mild TBI did not appreciably change this finding (data not shown). E-values suggest that moderate confounding would be required to explain away the observed associations (i.e., exposure/confounder and outcome/confounder relative risk >3.0; Appendix Table D.1).

Table 5.2. Proportion of hearing difficulty and probable PTSD by blast exposure, and hearing difficulty by probable PTSD

A. Exposure-Outcome

Blast	Hearing Difficulty		Unadjusted		Adjusted [a]	
	Yes	No	PPR	95% CI	PPR	95% CI
Yes	43 (38.1%)	70 (61.9%)	2.4	1.7, 3.4	2.0	1.3, 3.0
No	57 (15.7%)	307 (84.3%)	1.0	Ref	1.0	Ref

B. Exposure-Mediator

Blast	Probable PTSD		Unadjusted		Adjusted [a]	
	Yes	No	PPR	95% CI	PPR	95% CI
Yes	49 (43.4%)	64 (56.6%)	2.6	1.9, 3.6	1.8	1.3, 2.6
No	60 (16.5%)	304 (83.5%)	1.0	Ref	1.0	Ref

C. Mediator-Outcome

Probable PTSD	Hearing Difficulty		Unadjusted		Adjusted [b]	
	Yes	No	PPR	95% CI	PPR	95% CI
Yes	53 (48.6%)	56 (51.4%)	3.8	2.7, 5.3	3.1[†]	2.2, 4.3
No	47 (12.8%)	321 (87.2%)	1.0	Ref	1.0	Ref

Abbreviations: PPR, prevalence proportion ratio; CI, confidence interval; PTSD, post-traumatic stress disorder.

[a] Adjusted for sex, age, race/ethnicity, education, marital status, service branch, service component, service duration, and combat deployment.

[b] Adjusted for the above ([a]) plus blast exposure.

5.4.2. Mediation Analysis

The total blast - self-reported hearing difficulty association was partitioned into NDE and NIE mediated through PTSD (Table 5.3). The total association was attenuated after adjustment for demographic and service characteristics; despite adjustment, the point estimate remained elevated. The blast-hearing difficulty association was slightly larger for NDE than NIE. Results for the NDE (the effect that would be realized if the effect of blast exposure on PTSD had been blocked) showed an association with hearing difficulty (NDE = 1.7; 95% CI: 1.1, 2.3). Results for the NIE (the effect that would be realized if the mediator, probable PTSD, were somehow changed to what it would be without blast exposure) also showed an association with hearing difficulty (1.3; 95% CI: 1.0, 1.5). We estimate that just over 41% (95% CI: 17, 66%) of the total association was mediated through probable PTSD.

Table 5.3. Estimated direct and indirect (through PTSD) associations of blast exposure on self-reported hearing difficulty

	Unadjusted		Adjusted [a]	
	PPR	95% CI	PPR	95% CI
Total Effect	2.4	1.6, 3.2	2.2	1.4, 3.0
Natural Direct Effect	1.8	1.1, 2.5	1.7	1.1, 2.3
Natural Indirect Effect	1.4	1.1, 1.6	1.3	1.0, 1.5
Proportion Mediated	45%	18, 72%	41%	17, 66%

Abbreviations: PPR, prevalence proportion ratio; CI, confidence interval; PTSD, post-traumatic stress disorder

[a] Adjusted for sex, age, race/ethnicity, education, marital status, service branch, service component, service duration, and combat deployment.

Results of the four-way decomposition analysis are reported in Table 5.4, which provides further insight into the composition of the total association between blast exposure and self-reported hearing difficulty, namely by parsing out the contribution of a potential interaction and mediation between blast exposure and probable PTSD. In the fully adjusted model, the CDE, which estimates the effect between blast exposure and hearing difficulty, excluding the average effect of PTSD, was approximately 54% of the total association. The PIE, which estimates the effect due to mediation by probable PTSD and not interaction, was approximately 37% of the total association. There was no indication of either a reference or mediated interaction between blast exposure and probable PTSD.

When the respective components are combined, interaction (reference interaction + mediated interaction) accounts for approximately 9% of the total effect and appears negligible. The estimated e-value was 1.9, suggesting that moderate confounding would be required to explain away the observed natural indirect association (Appendix Table D.1).

Table 5.4. Percent decomposition of the observed direct and indirect associations of blast exposure on self-reported hearing difficulty

	Unadjusted		Adjusted [a]	
	% Mediated	95% CI	% Mediated	95% CI
Controlled Direct	49%	12, 87%	54%	18, 90%
Reference Interaction	6%	-10, 22%	4%	-16, 25%
Mediated Interaction	10%	-15, 35%	5%	-17, 27%
Pure Indirect	35%	12, 58%	37%	10, 63%

Abbreviations: %, percent; CI, confidence interval.
Percent (%) mediated and 95% CI are displayed.
[a] Adjusted for sex, age, race/ethnicity, education, marital status, service branch, service component, service duration, and combat deployment.

5.5. Discussion

We examined blast exposure and self-reported hearing difficulties among post-9/11 military Service members and Veterans with normal peripheral hearing and addressed the potential mediating role of PTSD in this population. We found that individuals with blast exposure had higher prevalence of probable PTSD and self-reported hearing difficulty than individuals without blast exposure. Our finding that blast exposure was associated with self-reported hearing difficulty among Service members and Veterans without peripheral hearing loss is generally consistent with the previous literature and what has been observed anecdotally in VA audiology clinics.[14,15,62,130] We also found that individuals with probable PTSD and normal peripheral hearing had higher prevalence of self-reported hearing difficulty than individuals without probable PTSD. Service members and Veterans with probable PTSD had a 3-fold higher prevalence of self-reported hearing difficulty compared to individuals without probable PTSD, after adjusting for potential confounders including blast. This is a unique contribution to the literature and suggests that PTSD may play an important role in the association between blast exposure and self-reported hearing difficulty. Formal mediation analysis suggested that a high proportion of the blast – self-reported hearing difficulty association was mediated by PTSD (41%). This finding has important clinical implications. Individuals with normal hearing who complain of hearing difficulties may benefit by evaluation for untreated PTSD symptoms and referred to mental health care when warranted.

We extended previous observational studies of blast exposure and hearing difficulty by estimating the mediating role of PTSD. We report a direct association between blast exposure and hearing difficulty, and an indirect association occurring through probable PTSD. There was little support for interactive effects within the mediation framework. These findings suggest a chain of risk, whereby one exposure contributes to subsequent exposures and each adverse experience raises the risk of the outcome (without the links on the chain interacting). These results support the conceptual framework that suggests PTSD may lead to poor health outcomes through psychological and attentional mechanisms that alter symptom perception.[99] Thus, individuals with PTSD are more likely to report poor health in the absence of disease/injury compared to individuals without PTSD. By understanding this risk process, interventions can be directed toward mediating factors as well as the primary exposure itself. This perspective may also be helpful when considering the complex health outcomes of war-related exposures.

The presence of PTSD mediation does not rule out concomitant auditory processing difficulties among participants. Considering the magnitude of the observed mediation, our results suggest the association between blast exposure and self-reported hearing difficulty among those with normal hearing may also be mediated through other pathways. From an audiologic perspective, possible mechanisms include sub-clinical damage to the cochlea (i.e., undetectable peripheral hearing loss)[40] and central auditory nervous system dysfunction (i.e., at the level of the brainstem and higher).[16,61] Some early evidence exists to support each of these mechanisms, although prospective studies capable of empirically testing such mediation are lacking. From a mental health perspective, other possible mechanisms and factors include depression, addiction, and non-PTSD-related anxiety. Each of these potential contributors warrants further investigation. Investigators wishing to further explore these mechanisms should utilize a causal framework to clearly identify hypothesized causal relationships. Explicit causal relationships coupled with clear causal questions will help to elucidate potential effects of blast exposure on auditory function.[147]

The main strength of this study lies in its use of an explicit causal framework based on theory and prior knowledge. We investigated each segment of the hypothesized pathway including assessment of mediation, which helps to advance discovery from association toward causality and mechanistic understanding. Limitations include the use of self-rating/reporting for the exposure, mediator, and outcome variables, complete-case analysis, and the lack of a longitudinal data structure. Conclusions regarding causality are constrained because of the cross-sectional study design that precludes establishing temporality. Further, even when using a causal mediation framework, it is unclear whether results estimated in existing data will translate into actual effects of potential future interventions (i.e., transportability is unknown).[148] Policymakers should be cautious in applying results of this and other studies to different, non-study contexts (including the same system at a different time); inverse probability of sampling weights could be used to assess transportability.[148]

Notwithstanding these caveats, our findings have possible clinical implications both in the war theater and in audiology clinics. For individuals exposed to blasts, early interventions for stress reduction to mitigate the onset of PTSD may be an important focus. In the clinic, audiologists should consider screening for PTSD with appropriate referrals to mental health when warranted for Service members and Veterans with normal peripheral hearing who report hearing difficulty. Integrated treatment protocols that address both PTSD and hearing difficulty would also be helpful.

Chapter 6. Discussion

6.1. Summary

Presented in this dissertation are a series of epidemiologic studies centered around hearing health in post-9/11 Veterans. The overall objective of this dissertation was to provide empirical data on the burden and mechanisms of adverse hearing outcomes among post-9/11 Service members and Veterans. An important first step was the characterization of the prevalence of hearing loss among recently separated Veterans using VA health care. This was followed by an investigation of the potential causes and mechanisms that may contribute to early hearing changes in the auditory system and their consequences. In doing so, novel methods were selected to help address some of the existing limitations in the literature. Acquiring foundational knowledge about exposures and hearing outcomes is the first step to informing hearing loss prevention efforts and informing military service-related rehabilitation and compensation practices.

In Chapter 3 (Aim 1), the results of the Bayesian hierarchical analysis suggest 1 in 10 recently separated post-9/11 Veterans coming into the VA health care system have hearing loss in the speech frequency range. Most hearing losses were predicted to be mild. In listening in quiet conditions, mild hearing loss generally is not problematic but can become a substantial barrier to communication when in the presence of background noise and complex acoustic environments. Mild hearing loss is also associated with poorer physical health such as history of falling and cognitive decline – both of which are major sources of morbidity and death among older adults and generate billions in health care costs annually. Moreover, communication difficulty, fall risk, and cognitive decline all increase as hearing loss progresses from mild to severe. Thus, primary and secondary prevention strategies to mitigate hearing loss are necessary to assure military personnel and Veteran health.

Given the high burden of hearing loss among recently separated Veterans, the next logical step was to investigate potential risk factors for incipient hearing changes. In Chapter 4 (Aim 2), we examined the impact of military occupations with a low, moderate, and high noise exposure ranking on the longitudinal trajectory of hearing thresholds by frequency. Rate of hearing-threshold change might be especially relevant, given the link between early noise exposures and accelerated age-related hearing loss later in life.[123,124] Using a hierarchical linear model, we found that the average annual rate of hearing change varied by military occupation classification (low, moderate, and high noise exposure rank), service branch, and audiometric frequency. The greatest rates of change were noted in the higher frequencies consistent with noise exposure patterns observed historically in the audiogram. Importantly, we found that the average annual rate of hearing change among Marine Corps personnel in occupations with a high noise exposure ranking suggests hearing may be declining at a faster rate than what would be expected for their age group. We also noted Army personnel with moderate noise exposure rankings displayed meaningful rates of hearing threshold change on average, though less than the Army and Marine Corps groups with high noise exposure rankings. The difference in hearing threshold changes across the branches and noise exposure rankings is likely indicative of the varying types of noise these groups are exposed to and, importantly, varying polices on hearing loss surveillance and hearing protection device use and enforcement. This suggests continued efforts should be made to improve hearing protection device selection, fit-testing, and training in the use of individually fitted protection. Taken together, aims 1 and 2 of this work highlight the need for continued promotion of hearing health, workplace hearing loss prevention efforts, and early intervention.

While Chapter 4 (Aim 2) focused on occupational noise as the exposure, Chapter 5 (Aim 3) focused on blasts as an exposure. The blast itself is a common source of impulse noise that can result in physical injury to the middle and inner ear. The blast wave is also known to cause physical injury to the auditory structures in the brainstem and brain, often by way of a traumatic brain injury. These injuries to the auditory system (from ear to cortex) are often used to explain Veterans' complaints of hearing difficulty despite having normal or near-normal hearing thresholds. However, other causal mechanisms are likely to exist outside the auditory system and to date have not been investigated. Veterans exposed to blasts are often diagnosed with PTSD. Though never formally tested, we theorized that PTSD may alter symptom perception, such as reporting hearing difficulty in the absence of hearing impairment and thus, PTSD may be a mediator in the association between blast and self-reported hearing difficulty. We examined this potential pathway in Chapter 5 (Aim 3). For the first time, we have documented that, compared to individuals without PTSD, those with probable PTSD had a higher prevalence of self-reported hearing difficulty. Additionally, using a formal causal mediation framework, we found that a high proportion (41%) of the observed association between blast exposure and self-reported hearing difficulty was mediated by a positive screen for PTSD. We believe that these results have high potential to affect current audiologic practice in military and VA health care settings. Given that blast exposure may not be preventable, but PTSD may be, individuals with normal hearing who complain of hearing difficulties may benefit from evaluation for PTSD symptoms and referred to mental health care when warranted.

Collectively, this body of work highlights opportunities for workplace hearing loss prevention and early intervention to mitigate hearing loss and its consequences. Addressing work-related exposures and subsequent injuries, illnesses, and disabilities is important for ensuring a healthy military and Veteran community. Hazardous levels of noise and blast exposures have adverse effects on Service members' hearing health and place a substantial financial burden on the DoD and VA. A deeper understanding of the health burden, magnitude of hearing changes, and mechanisms of auditory injuries will aid the DoD in designing more effective interventions and improve the occupational health of Service members. Improving our knowledge of Service members' health helps fulfill our duty to "care for those who have borne the battle" and ensure Service members' long-term health and wellbeing.

6.2. Methodologic strengths and challenges addressed

The existing literature regarding hearing loss burden in recently separated Veterans is scarce and relies on administrative health care records tethered to Veterans actively seeking health care, namely an audiology clinical encounter. As such, many Veterans do not have hearing thresholds available to summarize the hearing loss burden. In Chapter 2, we use Bayesian logic in a hierarchical framework to construct a model with primary collected research data to predict hearing thresholds in our sample of Veterans without hearing tests. This approach improves the methodological sophistication of administrative health care records to inform the burden of hearing loss by considering the entire sample of Veterans and by presenting the prevalence estimate of hearing loss with a probability interval. This approach has utility in other research applications which seek to understand the burden of disease or disability. As a further methodologic point of significance, previous studies have relied on collapsing hearing information into binary yes/no categories. We preserved the hearing information encoded by threshold and frequency in our estimates of hearing loss prevalence (e.g., mild, moderate, severe) and magnitude of hearing change. Exploiting threshold and frequency information enriches our understanding of the impacts of military exposures on hearing and can also be used to inform resource allocation.

Assessment of mediation is an important, and to-date under-utilized, tool for exploring the mechanisms that underlie audiologic exposure-outcomes associations. Moving beyond the dominant paradigm of mediation analysis (i.e., adjustment for the mediator), which can produce biased estimates unless strict assumptions and model forms are met, we utilized a novel causal framework approach to mediation analysis, thus moving from associations toward causality and mechanistic understanding. An improved understanding of mechanisms that mediate an association highlights a new potential target for intervention – such knowledge is particularly helpful when the exposure itself is non-modifiable, which is the case for many war-related exposures.

6.3. The advantage of linkage with NOISE Study data

This dissertation utilized research data collected as part of an ongoing longitudinal study on military exposures and hearing among Veterans. The NOISE Study is a rich source of data for this dissertation, as it allowed for a more granular examination of a well characterized group of Veterans and Service members. The NOISE Study provided rigorous audiologic examinations and in-depth surveys on an individual's military history and exposures; perceived auditory, mental, and physical health; and quality of life. As such, we were able to address underlying knowledge gaps in the military hearing science literature. For example, we were able to provide the first estimate of the prevalence of hearing loss among recently separated Veterans who use VA health care by developing a prediction model using the NOISE Study data (Chapter 3). This was important because we only found 20% of Veterans in the VA administrative health care database to have a hearing test to inform our estimates of prevalence. Additionally, the linkage between the NOISE Study and the DoD DOEHRS-HC data repository (Chapter 4) provided the opportunity to examine key differences in the average annual rate of hearing change by service branch and cumulative occupational noise exposure ranking that would not have been possible with either dataset alone.

6.4. Public health impact

Overall, the findings from this dissertation have clear and important implications for audiologic practice that aims to reduce population-level hearing impairment and its consequences. We found that some Service members are at risk for accelerated hearing decline based on their presumed occupational noise exposure. Furthermore, we found a significant burden of hearing loss among recently separated Veterans coming into the VA health care system. Coupled together, this suggests our efforts should be placed on hearing loss prevention while in the military and early identification and intervention when transitioning to care within the VA health care system. Currently, the DoD is responsive to auditory health and has a robust and growing hearing conservation program. However, newly separated Veterans entering the VA health care system are not screened for hearing loss. Despite Veterans enrolled in VA health care having unfettered access to audiologic care, we found only 20% of Veterans had an audiology clinical encounter within 2.5 years of service separation. We observed 13,743 Veterans with a hearing loss among those with a hearing test but estimate that anywhere between 36,839 and 94,687 recently separated Veterans actually had hearing loss – meaning 63-85% of Veterans with hearing loss did not receive audiologic care at the VA shortly after separating from military service. This suggests Veteran awareness of hearing loss and its consequences is likely to be low.

The lack of a perceived need and seeking timely care can be placed within the context of a public health framework. From the Veteran perspective, perceiving a need and seeking care is likely due to several factors. First is the awareness in the general community as well as the medical community regarding the adverse effects and impacts of untreated hearing loss and the potential treatment options. It may also reflect a low prioritization by the patient and the provider against other health needs. The perceived need may also be tied to the severity of the hearing loss. Knowing that early intervention is key to treatment and the prevention of further decline, it is imperative that individuals with hearing loss not only seek help but do so early and are presented with hearing health education, rehabilitation (when warranted) and communication strategies. Thus, public health strategies to inform, educate, and screen Veterans for hearing loss are needed in the VA health care system to mitigate hearing loss when it has occurred and to prevent its downstream, lifelong effects. We hope that publication of this work will lead to continued efforts to preserve hearing in Service members and earlier identification and management of hearing loss among Veterans who use VA for their health care needs.

Lastly, we found that PTSD may be mediating a portion of the observed associations between blast exposure and self-reported hearing difficulty among audiometrically normal Service members and Veterans. This has clinical implications for the audiologist. Service members and Veterans with hearing complaints who are considered otologically normal may benefit from a PTSD screen by the audiologist. While only a mental health care provider can diagnosis PTSD, a screening can help the audiologist understand if the individual would benefit from treatment and onward referral. These findings highlight the need and opportunity for coordinated health care services between audiology and mental health. A coordinated approach could lead to better health through enhanced access to services, improved quality and timeliness of care, and potentially lower overall health care costs.

6.5. Limitations point to future research needs

This body of work was not without limitations (described toward the end of Chapters 3-5). Issues such as sample size, generalizability, imperfect measures, and study design were noted. However, while the limitations raise awareness about shortcomings of the work, it also informs theoretical and methodological areas for future research. First, small cell counts were evident in the prediction model used to inform our estimate of the prevalence of hearing loss among recently separated Veterans. These estimates could be improved upon by targeted recruiting of individuals from particular respondent subtypes that suffered from small cell counts and refitting the model. A logical next step would be to validate this prediction model in a random sample of VA users. While we advocate for population-based hearing screening among recently separated Veterans, the feasibility, acceptability to Veterans, ability to identify those with hearing loss, and referring for audiologic services need to be explored.

The accuracy of the estimated relationship between noise exposures and hearing outcomes is dependent on the quality of the noise exposure assessment. Capturing military noise exposure is especially challenging because of the acoustically diverse environments and complex noise exposure patterns. Furthermore, dosimetry occupational data are not readily available, forcing exposure assessment to be ascertained by self-report or through expert opinion. Self-reported retrospective exposure assessment for epidemiologic purposes adds another layer of measurement complexity and introduces subtleties and avenues for bias that are absent in objective measures. Therefore, a job exposure matrix created using expert judgment, aided by quantitative measures, published literature and communication with industry personnel is necessary to advance our understanding of military hearing health outcomes in the short and long terms. Efforts should also be directed toward refining the self-reported blast measures.

Findings from Chapter 5 support the need for further study into the other auditory and non-auditory mechanisms underlying the blast – self-reported hearing difficulty association. Auditory mechanisms might involve measurement of the auditory nerve connections with the cochlear hair cells and central auditory function. How the auditory and non-auditory pathways might interact to synergistically increase complaints of hearing difficulty should also be considered. This work should be carried out in a longitudinal study design. Additionally, data from future investigations of the effects of a PTSD intervention on self-reported hearing difficulty are needed. These additional data will allow for more definitive guidance to treatment and management of blast-exposed individuals with normal hearing but self-report hearing difficulty.

6.6. Conclusions

Taken together, this body of work has begun urgently needed epidemiologic analyses of the complex relationships between noise and blast exposures and hearing outcomes in post-9/11 Veterans. First, we described the burden of hearing loss among recently separated Veterans. Next, we estimated the longitudinal rates of hearing change among military personnel and noted rates were influenced by occupational determinants. Finally, we found PTSD to mediate a large proportion of the blast – self-reported hearing difficulty association; as such, interventions targeting PTSD may have added value in mitigating hearing complaints in noise. Continued efforts to elucidate the impact of noise and blast exposure on hearing including the biologic mechanisms and public health impacts are necessary. The results from this dissertation will hopefully have a positive, albeit incremental, impact on the future of military hearing health.

References

1. Abel SM. Hearing loss in military aviation and other trades: investigation of prevalence and risk factors. *Aviation, Space, and Environmental Medicine* 2005;76(12):1128-35.

2. Yong JS, Wang DY. Impact of noise on hearing in the military. *Military Medical Research* 2015;2:6.

3. Dalton DS, Cruickshanks KJ, Klein BE, Klein R, Wiley TL, Nondahl DM. The impact of hearing loss on quality of life in older adults. *The Gerontologist* 2003;43(5):661-8.

4. Gallacher J, Ilubaera V, Ben-Shlomo Y, Bayer A, Fish M, Babisch W, Elwood P. Auditory threshold, phonologic demand, and incident dementia. *Neurology* 2012;79(15):1583-90.

5. Department of Veterans Affairs. VBA Annual Benefits Report Fiscal Year 2019 - Compensation.Available from: https://www.benefits.va.gov/REPORTS/abr/docs/2019-abr-v2.pdf# (Accessed September 12, 2020).

6. McArdle R. Update on the VA Audiology Program [Conference presentation]. *Joint Defense Veterans Audiology Conference 2020, Rosemont, IL, United States* 2020, February 10-12.

7. Yankaskas K, Hammill T, Packer M, Zuo J. Editorial: Auditory injury - A military perspective. *Hearing Research* 2017;349:1-3.

8. Yankaskas K. Prelude: noise-induced tinnitus and hearing loss in the military. *Hearing Research* 2013;295:3-8.

9. Humes LE, Joellenbeck LM, Durch JS, eds. Noise and military service: Implications for hearing loss and tinnitus. Washington, DC: The National Academies Press, 2006.

10. Joseph AR, Shaw JL, Clouser MC, MacGregor AJ, Dougherty AL, Galarneau MR. Clinical audiometric patterns of hearing loss following blast-related injury in U.S. military personnel. *International Journal of Audiology* 2020:1-8.

11. Joseph AR, Shaw JL, Clouser MC, MacGregor AJ, Galarneau MR. Impact of Blast Injury on Hearing in a Screened Male Military Population. *American Journal of Epidemiology* 2018;187(1):7-15.

12. Mathews ZR, Koyfman A. Blast Injuries. *The Journal of Emergency Medicine* 2015;49(4):573-87.

13. Elsayed NM. Toxicology of blast overpressure. *Toxicology* 1997;121:1-15.

14. Saunders GH, Frederick MT, Arnold M, Silverman S, Chisolm TH, Myers P. Auditory difficulties in blast-exposed Veterans with clinically normal hearing. *Journal of Rehabilitation Research and Development* 2015;52(3):343-60.

15. Bressler S, Goldberg H, Shinn-Cunningham B. Sensory coding and cognitive processing of sound in Veterans with blast exposure. *Hearing Research* 2017;349:98-110.

16. Gallun FJ, Lewis MS, Folmer RL, Diedesch AC, Kubli LR, McDermott DJ, Walden TC, Fausti SA, Lew HL, Leek MR. Implications of blast exposure for central auditory function: A review. *Journal of Rehabilitation Research and Development* 2012;49(7):1059.

17. Department of Veterans Affairs. National Center for Veterans Analysis and Statistics, Veteran Population, Population Tables, The Nation, Period Served. .Available from https://www.va.gov/vetdata/Veteran_Population.asp (Accessed September 11, 2020).

18. Holder KA. Veterans Who Have Served Since 9/11 Are More Diverse. 2018;Available from: https://www.census.gov/library/stories/2018/04/post-9-11-veterans.html. (Accessed August 29, 2020).

19. Price GR, Kalb JT, Garinther GR. Toward a measure of auditory handicap in the Army. *Annals of Otology, Rhinology & Laryngology Supplement* 1989;140:42-52.

20. Niebuhr DW, Li Y, Powers TE, Krauss MR, Chandler D, Helfer T. Attrition of U.S. military enlistees with waivers for hearing deficiency, 1995-2004. *Military Medicine* 2007;172(1):63-9.

21. Morata TC, Themann CL, Randolph RF, Verbsky BL, Byrne DC, Reeves ER. Working in noise with a hearing loss: perceptions from workers, supervisors, and hearing conservation program managers. *Ear and Hearing* 2005;26(6):529-45.

22. Ruben RJ. Redefining the Survival of the Fittest: Communication Disorders in the 21st Century. *The Laryngoscope* 2000;110:241-245.

23. Shan A, Ting JS, Price C, Goman AM, Willink A, Reed NS, Nieman CL. Hearing loss and employment: a systematic review of the association between hearing loss and employment among adults. *The Journal of Laryngolgy & Otology* 2020;134(5):387-397.

24. Jung D, Bhattacharyya N. Association of hearing loss with decreased employment and income among adults in the United States. *Annals of Otology, Rhinology & Laryngology* 2012;121(12):771-5.

25. Appollonio I, Carabellese C, Frattola L, Trabucchi M. Effects of sensory aids on the quality of life and mortality of elderly people: a multivariate analysis. *Age and Ageing* 1996;25(2):89-96.

26. Carabellese C, Appollonio I, Rozzini R, Bianchetti A, Frisoni GB, Frattola L, Trabucchi M. Sensory impairment and quality of life in a community elderly population. *Journal of the American Geriatrics Society* 1993;41(4):401-7.

27. Mulrow CD, Aguilar C, Endicott JE, Tuley MR, Velez R, Charlip WS, Rhodes MC, Hill JA, DeNino LA. Quality-of-life changes and hearing impairment. A randomized trial. *Annals of Internal Medicine* 1990;113(3):188-94.

28. Saunders GH, Griest SE. Hearing loss in veterans and the need for hearing loss prevention programs. *Noise & Health* 2009;11(42):14-21.

29. Fausti SA, Wilmington DJ, Helt PV, Helt WJ, Konrad-Martin D. Hearing health and care: The need for improved hearing loss prevention and hearing conservation practices. *The Journal of Rehabilitation Research and Development* 2005;42(4s):45.

30. Cacciatore F, Napoli C, Abete P, Marciano E, Triassi M, Rengo F. Quality of life determinants and hearing function in an elderly population: Osservatorio Geriatrico Campano Study Group. *Gerontology* 1999;45(6):323-8.

31. Lin FR. Hearing loss and cognition among older adults in the United States. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences* 2011;66(10):1131-6.

32. Lin FR, Ferrucci L. Hearing loss and falls among older adults in the United States. *Archives of Internal Medicine* 2012;172(4):369-71.

33. Lin FR, Ferrucci L, An Y, Goh JO, Doshi J, Metter EJ, Davatzikos C, Kraut MA, Resnick SM. Association of hearing impairment with brain volume changes in older adults. *NeuroImage* 2014;90:84-92.

34. Lin FR, Ferrucci L, Metter EJ, An Y, Zonderman AB, Resnick SM. Hearing loss and cognition in the Baltimore Longitudinal Study of Aging. *Neuropsychology* 2011;25(6):763-70.

35. Genther DJ, Betz J, Pratt S, Martin KR, Harris TB, Satterfield S, Bauer DC, Newman AB, Simonsick EM, Lin FR, Health A, Body Composition S. Association Between Hearing Impairment and Risk of Hospitalization in Older Adults. *Journal of the American Geriatrics Society* 2015;63(6):1146-52.

36. Genther DJ, Frick KD, Chen D, Betz J, Lin FR. Association of hearing loss with hospitalization and burden of disease in older adults. *Journal of the American Medical Association* 2013;309(22):2322-4.

37. Lin HW, Mahboubi H, Bhattacharyya N. Self-reported Hearing Difficulty and Risk of Accidental Injury in US Adults, 2007 to 2015. *JAMA Otolaryngolgy - Head & Neck Surgery* 2018;144(5):413-417.

38. Abrams TE, Barnett MJ, Hoth A, Schultz S, Kaboli PJ. The relationship between hearing impairment and depression in older veterans. *Journal of the American Geriatrics Society* 2006;54(9):1475-7.

39. Mulrow CD, Aguilar C, Endicott JE, Velez R, Tuley MR, Charlip WS, Hill JA. Association between hearing impairment and the quality of life of elderly individuals. *Journal of the American Geriatrics Society* 1990;38(1):45-50.

40. Kujawa SG, Liberman MC. Adding insult to injury: cochlear nerve degeneration after "temporary" noise-induced hearing loss. *Journal of Neuroscience* 2009;29(45):14077-85.

41. Kujawa SG, Liberman MC. Synaptopathy in the noise-exposed and aging cochlea: Primary neural degeneration in acquired sensorineural hearing loss. *Hearing Research* 2015;330(Pt B):191-9.

42. Liberman LD, Suzuki J, Liberman MC. Dynamics of cochlear synaptopathy after acoustic overexposure. *Journal of the Association for Research in Otolaryngology* 2015;16(2):205-19.

43. Bramhall NF, Konrad-Martin D, McMillan GP, Griest SE. Auditory Brainstem Response Altered in Humans With Noise Exposure Despite Normal Outer Hair Cell Function. *Ear and Hearing* 2017;38(1):e1-e12.

44. Wang Y, Hirose K, Liberman MC. Dynamics of noise-induced cellular injury and repair in the mouse cochlea. *Journal of the Association for Research in Otolaryngology* 2002;3(3):248-68.

45. Centers for Disease Control and Prevention. Loud Noise Can Cause Hearing Loss: How Does Loud Noise Cause Hearing Loss? ;Available from: https://www.cdc.gov/nceh/hearing_loss/how_does_loud_noise_cause_hearing_loss.html#:~:text=Loud%20noise%20can%20damage%20cells,long%20as%20the%20exposure%20continues. (Accessed September 9, 2018).

46. Roberto M, Hamernik RP, Turrentine GA. Damage of the auditory system associated with acute blast trauma. *Annals of Otology, Rhinology & Laryngology Supplement* 1989;140:23-34.

47. Patterson JH, Jr., Hamernik RP. Blast overpressure induced structural and functional changes in the auditory system. *Toxicology* 1997;121(1):29-40.

48. Garth RJ. Blast injury of the auditory system: a review of the mechanisms and pathology. *The Journal of Laryngology & Otology* 1994;108(11):925-9.

49. Cave KM, Cornish EM, Chandler DW. Blast injury of the ear: clinical update from the global war on terror. *Military Medicine* 2007;172(7):726-30.

50. Saunders GH, Echt KV. Blast exposure and dual sensory impairment: an evidence review and integrated rehabilitation approach. *Journal of Rehabilitation Research and Development* 2012;49(7):1043-58.

51. Institute of Medicine. Gulf War and Health: Long-term effects of blast exposure. Vol. 9. Washington, DC: National Academies Press, 2014.

52. Ritenour AE, Wickley A, Ritenour JS, Kriete BR, Blackbourne LH, Holcomb JB, Wade CE. Tympanic membrane perforation and hearing loss from blast overpressure in Operation Enduring Freedom and Operation Iraqi Freedom wounded. *The Journal of Trauma* 2008;64(2 Suppl):S174-8; discussion S178.

53. Yeh DD, Schecter WP. Primary blast injuries--an updated concise review. *World Journal of Surgery* 2012;36(5):966-72.

54. Greer N, Sayer N, Kramer M, Koeller E, Velasquez T. VA Evidence-based Synthesis Program Reports. *Prevalence and Epidemiology of Combat Blast Injuries from the Military Cohort 2001-2014*. Washington (DC): Department of Veterans Affairs (US), 2016.

55. Belmont PJ, Jr., McCriskin BJ, Sieg RN, Burks R, Schoenfeld AJ. Combat wounds in Iraq and Afghanistan from 2005 to 2009. *Journal of Trauma and Acute Care Surgery* 2012;73(1):3-12.

56. Regasa LE, Agimi Y, Stout KC. Traumatic Brain Injury Following Military Deployment: Evaluation of Diagnosis and Cause of Injury. *The Journal of Head Trauma Rehabilitation* 2019;34(1):21-29.

57. Department of Defense. Casualty Status as of 10am EDT Sep 28, 2020. 2020;Available from: https://www.defense.gov/casualty.pdf. (Accessed October 4, 2020).

58. Defense Medical Surveillance System. 2000-2019 DoD Numbers for Traumatic Brain Injury Worldwide - Totals. 2020;Available from: https://health.mil/Military-Health-Topics/Conditions-and-Treatments/Physical-Disability/Traumatic-Brain-Injury?type=All#RefFeed (Accessed on October 4, 2020).

59. Rafaels K, Bass CR, Salzar RS, Panzer MB, Woods W, Feldman S, Cummings T, Capehart B. Survival risk assessment for primary blast exposures to the head. *Journal of Neurotrauma* 2011;28(11):2319-28.

60. Gondusky JS, Reiter MP. Protecting military convoys in Iraq: an examination of battle injuries sustained by a mechanized battalion during Operation Iraqi Freedom II. *Military Medicine* 2005;170(6):546-9.

61. Tepe V, Papesh M, Russell S, Lewis MS, Pryor N, Guillory L. Acquired Central Auditory Processing Disorder in Service Members and Veterans. *Journal of Speech, Language, and Hearing Research* 2020;63(3):834-857.

62. Gallun F, Lewis MS, Folmer RL, Hutter M, Papesh MA, Belding H, Leek MR. Chronic effects of exposure to high-intensity blasts: Results of tests of central auditory processing. *Journal of Rehabilitation Research & Development* 2016;53(5):705-720.

63. Gallun FJ, Papesh MA, Lewis MS. Hearing complaints among veterans following traumatic brain injury. *Brain Injury* 2017;31(9):1183-1187.

64. Institute of Medicine. *Noise and Military Service: Implications for Hearing Loss and Tinnitus*. Washington, DC: The National Academies Press, 2006.

65. Helfer T, Beamer S, Deaver K, Hall S. Active Duty – U. S. Army Noise Induced Hearing Injury Surveillance Annual Calendar Year 2009-2013. 2014; Available from: http://www.dtic.mil/dtic/tr/fulltext/u2/1013106.pdf (Accessed August 15, 2018).

66. Helfer TM, Jordan NN, Lee RB, Pietrusiak P, Cave K, Schairer K. Noise-induced hearing injury and comorbidities among postdeployment U.S. Army soldiers: April 2003-June 2009. *American Journal of Audiology* 2011;20(1):33-41.

67. Department of Defense Hearing Conservation Working Group. Hearing Health Surveillance Data Review Military Hearing Conservation - CY18 Department of Defense Hearing Center of Excellence, 2020.

68. Hammill TL, Esquivel CR. Role of the US Department of Defense Hearing Center of Excellence in Studying the Treatment of Tinnitus. *JAMA Otolaryngology - Head & Neck Surgery* 2019;145(7):608-609.

69. Nelson JT, Swan AA, Swiger B, Packer M, Pugh MJ. Hearing testing in the U.S. Department of Defense: Potential impact on Veterans Affairs hearing loss disability awards. *Hearing Research* 2017;349:13-20.

70. Military Health System. Defense Occupational and Environmental Health Readiness System – Hearing Conservation 2013; Available from:

https://health.mil/Military-Health-Topics/Technology/Clinical-Support/Centralized-Credentials-Quality-Assurance-System/Decision-Support/DOEHRS-HC (Accessed October 28, 2018).

71. Department of Veterans Affairs. Profile of Post-9/11 Veterans: 2016 Available from: https://www.va.gov/vetdata/docs/specialreports/post_911_veterans_profile_2016.pdf. (Accessed October 28, 2018).

72. Barroso A. The changing profile of the U.S. military: Smaller in size, more diverse, more women in leadership. 2019;Available from: https://www.pewresearch.org/fact-tank/2019/09/10/the-changing-profile-of-the-u-s-military/ (Accessed September 13, 2020).

73. Under Secretary of Defense for Acquisition TaL, Defense Science Board Task Force. Deployment of Members of the National Guard and Reserve in the Global War on Terrorism. 2007; Available from: https://www.acq.osd.mil/dsb/reports/2000s/ADA478163.pdf (Accessed: October 30, 2018).

74. Centers for Disease Control and Prevention. Severe hearing impairment among miliary Veterans - United States, 2010. *Morbidity and Mortality Weekly Report* 2011;60(28):955-8.

75. Wells TS, Seelig AD, Ryan MA, Jones JM, Hooper TI, Jacobson IG, Boyko EJ. Hearing loss associated with US military combat deployment. *Noise and Health* 2015;17(74):34-42.

76. Theodoroff SM, Lewis MS, Folmer RL, Henry JA, Carlson KF. Hearing impairment and tinnitus: prevalence, risk factors, and outcomes in US service members and veterans deployed to the Iraq and Afghanistan wars. *Epidemiologic Reviews* 2015;37:71-85.

77. Department of Veterans Affairs. VBA Annual Benefits Report Fiscal Year 2017 - Compensation Available from: https://benefits.va.gov/REPORTS/abr/docs/FY17-Compensation.pdf. (Accessed August 15, 2018).

78. Frayne SM, Chiu VY, Iqbal S, Berg EA, Laungani KJ, Cronkite RC, Pavao J, Kimerling R. Medical care needs of returning veterans with PTSD: their other burden. *Journal of General Internal Medicine* 2011;26(1):33-9.

79. Swan AA, Nelson JT, Swiger B, Jaramillo CA, Eapen BC, Packer M, Pugh MJ. Prevalence of hearing loss and tinnitus in Iraq and Afghanistan Veterans: A Chronic Effects of Neurotrauma Consortium study. *Hearing Research* 2017;349:4-12.

80. Surján G. Questions on validity of International Classification of Diseases-coded diagnoses. *International Journal of Medical Informatics* 1999;54(2):77-95.

81. van Walraven C, Austin P. Administrative database research has unique characteristics that can risk biased results. *Journal of Clinical Epidemiology* 2012;65(2):126-31.

82. Department of Defense. DoD Instruction 6055.12 "DoD Hearing Conservation Program (HCP)". 2010;Available from: https://www.med.navy.mil/sites/nmcphc/Documents/nepmu-6/DODI-6055-12-Hearing-Con-Dec2010.pdf (Accessed October 28, 2019).

83. Department of Defense. DoD Instruction 6055.12 "DoD Hearing Conservation Program (HCP)". 2019;Available from: https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/605512p.pdf?ver=2019-08-14-073309-537 (Accessed October 28, 2019).

84. Department of Defense. DoD Instruction 6055.12 "DoD Hearing Conservation Program (HCP)". 2004;Available from: https://biotech.law.lsu.edu/blaw/dodd/corres/pdf/i605512_030504/i605512p.pdf (Accessed October 28, 2019).

85. Occupational Safety and Health Administration. Occupational noise exposure standard (29 CFR 1910.95). Available from: https://www.osha.gov/laws-regs/regulations/standardnumber/1910/1910.95 (Accessed October 28, 2018).

86. Terrio H, Brenner LA, Ivins BJ, Cho JM, Helmick K, Schwab K, Scally K, Bretthauer R, Warden D. Traumatic brain injury screening: preliminary findings in a US Army Brigade Combat Team. *The Journal of Head Trauma Rehabilitation* 2009;24(1):14-23.

87. Hoge CW, McGurk D, Thomas JL, Cox AL, Engel CC, Castro CA. Mild traumatic brain injury in U.S. Soldiers returning from Iraq. *New England Journal of Medicine* 2008;358(5):453-63.

88. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghan, mental health problems and barriers to care. *New England Journal of Medicine* 2004;351(13-22).

89. Taylor BC, Hagel EM, Carlson KF, Cifu DX, Cutting A, Bidelspach DE, Sayer NA. Prevalence and costs of co-occurring traumatic brain injury with and without psychiatric disturbance and pain among Afghanistan and Iraq War Veteran V.A. users. *Medical Care* 2012;50(4):342-6.

90. Carlson KF, Nelson D, Orazem RJ, Nugent S, Cifu DX, Sayer NA. Psychiatric diagnoses among Iraq and Afghanistan war veterans screened for deployment-related traumatic brain injury. *Journal of Traumatic Stress* 2010;23(1):17-24.

91. Shively SB, Horkayne-Szakaly I, Jones RV, Kelly JP, Armstrong RC, Perl DP. Characterisation of interface astroglial scarring in the human brain after blast exposure: a post-mortem case series. *The Lancet Neurology* 2016;15(9):944-953.

92. Verfaellie M, Lafleche G, Spiro A, Bousquet K. Neuropsychological outcomes in OEF/OIF veterans with self-report of blast exposure: associations with mental health, but not MTBI. *Neuropsychology* 2014;28(3):337-46.

93. Vasterling JJ, Duke LM, Brailey K, Constans JI, Allain AN, Jr., Sutker PB. Attention, learning, and memory performances and intellectual resources in Vietnam veterans: PTSD and no disorder comparisons. *Neuropsychology* 2002;16(1):5-14.

94. Vasterling JJ, Brailey K, Constans JI, Sutker PB. Attention and memory dysfunction in posttraumatic stress disorder. *Neuropsychology* 1998;12(1):125-33.

95. Hoge CW, Terhakopian A, Castro CA, Messer SC, Engel CC. Association of posttraumatic stress disorder with somatic symptoms, health care visits, and absenteeism among Iraq war veterans. *American Journal of Psychiatry* 2007;164(1):150-3.

96. Barrett DH, Doebbeling CC, Schwartz DA, Voelker MD, Falter KH, Woolson RF, Doebbeling BN. Posttraumatic stress disorder and self-reported physical health status among U.S. Military personnel serving during the Gulf War period: a population-based study. *Psychosomatics* 2002;43(3):195-205.

97. Boscarino JA. Diseases among men 20 years after exposure to severe stress: implications for clinical research and medical care. *Psychosomatic Medicine* 1997;59(6):605-14.

98. Schnurr PP, Green, B. L. Understanding Relationships Among Trauma, Posttraumatic Stress Disorder, and Health Outcomes. In: Schnurr PP, Green, B. L., ed. *Trauma and Health: Physical Health Consequences of Exposure to Extreme Stress*. Washington, DC: American Psychological Assocation, 2004.

99. Schnurr PP. Understanding Pathways from Traumatic Exposure to Physical Health. In: Schnyder U, Cloitre M, eds. *Eviden Based Treatments for Trauma-Related Psychological Disorders: A Practical Guide for Clinicians*. New York, NY: Springer, 2015;87-103.

100. Friedman MJ, McEwen, B. S. . Posttraumatic Stress Disorder, Allostatic Load, and Medical Illness. In: Schnurr PP, Green, B. L., ed. *Trauma and Health:*

Physical Health Consequences of Exposure to Extreme Stress. Washington, D.C.: American Psychological Assocation, 2004.

101. Reed NS, Altan A, Deal JA, Yeh C, Kravetz AD, Wallhagen M, Lin FR. Trends in Health Care Costs and Utilization Associated With Untreated Hearing Loss Over 10 Years. *JAMA Otolaryngology - Head & Neck Surgery* 2019;145(1):27-34.

102. Lin FR, Albert M. Hearing loss and dementia - who is listening? *Aging & Mental Health* 2014;18(6):671-3.

103. Department of Veterans Affairs. Analysis of VA Health Care Utilization among Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) Veterans.Available from: https://www.publichealth.va.gov/docs/epidemiology/healthcare-utilization-report-fy2015-qtr3.pdf#. (Accessed August 28, 2020).

104. Department of Veterans Affairs. Privacy Act; System of Records. *Federal Register* 2009;74(142):37093 - 37096.

105. Price LE, Shea K, Gephart S. The Veterans Affairs's Corporate Data Warehouse: Uses and Implications for Nursing Research and Practice. *Nursing Administration Quarterly* 2015;39(4):311-8.

106. Henry JA, Griest S, Reavis KM, Grush L, Theodoroff SM, Young S, Thielman EJ, Carlson KF. Noise Outcomes in Service Members Epidemiology (NOISE) Study: Design, Methods, and Baseline Results. *Ear and Hearing* 2020;in press.

107. American National Standards Institute. Specification for Audiometers, S3.6-1996. 1996.

108. Mathers C, Smith A, Concha M. Global burden of hearing loss in the year 2000. *World Health Organization* 2003; Available from: http://www.who.int/healthinfo/statistics/bod_hearingloss.pdf. (Accessed August 15, 2018).

109. Gelman A, Little TC. Poststratification Into Many Categories Using Hierarchical Logistic Regression. *Survey Methodology* 1997;23(2):127-135.

110. Little RJA. Post-Stratification: A Modeler's Perspective. *Journal of the American Statistical Assocation* 1993;88(423):1001-1012.

111. Park DK, Gelman A, Bafumi J. Bayesian Multilevel Estimation with Poststratification: State-Level Estimates from National Polls. *Political Analysis* 2004;12(4):375-385.

112. Downes M, Carlin JB. Multilevel Regression and Poststratification Versus Survey Sample Weighting for Estimating Population Quantities in Large Population Health Studies. *American Journal of Epidemiology* 2020;189(7):717-725.

113. Downes M, Gurrin LC, English DR, Pirkis J, Currier D, Spittal MJ, Carlin JB. Multilevel Regression and Poststratification: A Modeling Approach to Estimating Population Quantities From Highly Selected Survey Samples. *American Journal of Epidemiology* 2018;187(8):1780-1790.

114. Spiegelhalter DJ, Abrams KR, Myles JP. *Bayesian Approaches to Clinical Trials and Health-Care Evaluation*. West Sussex, England: John Wiley & Sons Ltd, 2004.

115. McMillan GP, Cannon JB. Bayesian Applications in Auditory Research. *Journal of Speech, Language, and Hearing Research* 2019;62(3):577-586.

116. Masterson EA, Bushnell PT, Themann CL, Morata TC. Hearing Impairment Among Noise-Exposed Workers - United States, 2003-2012. *Morbidity and Mortality Weekly Report* 2016;65(15):389-94.

117. Department of Veterans Affairs. Department of Veterans Affairs FY 2018 - 2024 Strategic Plan.Available from: https://www.va.gov/oei/docs/VA2018-2024strategicPlan.pdf. (Accessed August 29, 2020).

118. Weiskopf NG, Rusanov A, Weng C. Sick patients have more data: the non-random completeness of electronic health records. *AMIA Annual Symposium Proceedings* 2013;2013:1472-7.

119. Goldstein BA, Bhavsar NA, Phelan M, Pencina MJ. Controlling for Informed Presence Bias Due to the Number of Health Encounters in an Electronic Health Record. *American Journal of Epidemiology* 2016;184(11):847-855.

120. Reed NS, Altan A, Deal JA, Yeh C, Kravetz AD, Wallhagen M, Lin FR. Trends in Health Care Costs and Utilization Associated With Untreated Hearing Loss Over 10 Years. *JAMA Otolaryngology - Head & Neck Surgery* 2019;145(1):27-34.

121. Department of Defense. DoD Instruction 6055.12 "DoD Hearing Conservation Program (HCP)". 2010; Available from: https://www.med.navy.mil/sites/nmcphc/Documents/oem/dodi-6055-12.pdf (Accessed October 28, 2018).

122. Department of Defense (DoD). DoD Instruction 6055.12 "DoD Hearing Conservation Program (HCP)" 2019.

123. Gates GA, Schmid P, Kujawa SG, Nam B, D'Agostino R. Longitudinal threshold changes in older men with audiometric notches. *Hearing Research* 2000;141(1-2):220-228.

124. Kujawa SG, Liberman MC. Acceleration of age-related hearing loss by early noise exposure: evidence of a misspent youth. *The Journal of neuroscience : the official journal of the Society for Neuroscience* 2006;26(7):2115-2123.

125. US Government Accountability Office. Hearing loss prevention: improvements to DOD hearing conservation programs could lead to better outcomes. 2011; Available from: https://www.gao.gov/new.items/d11114.pdf (Accessed August 15, 2018).

126. Powers R. *Basic Training for Dummies*. Hoboken, NJ: Wiley Publishing, 2011.

127. Singer JD, Willett JB. *Applied Longitudinal Data Analysis: Modeling Change and Event Occurence*. New York: Oxford University Press, 2003.

128. Echt KV, Smith SL, Burridge AB, Spiro A, 3rd. Longitudinal changes in hearing sensitivity among men: the Veterans Affairs Normative Aging Study. *The Journal of the Acoustical Society of America* 2010;128(4):1992-2002.

129. Rabinowitz PM, Galusha D, Dixon-Ernst C, Slade MD, Cullen MR. Do ambient noise exposure levels predict hearing loss in a modern industrial cohort? *Occupational and Environmental Medicine* 2007;64(1):53-59.

130. Gallun F, Diedesch AC, Kubli LR, Walden TC, Folmer RL, Lewis MS, McDermott DJ, Fausti SA, Leek MR. Performance on tests of central auditory processing by individuals exposed to high-intensity blasts. *Journal of Rehabilitation Research & Development* 2012;49(7):1005-1024.

131. Vasterling JJ, Jacob SN, Rasmusson A. Traumatic Brain Injury and Posttraumatic Stress Disorder: Conceptual, Diagnostic, and Therapeutic Considerations in the Context of Co-Occurrence. *The Journal of Neuropsychiatry and Clinical Neurosciences* 2018;30(2):91-100.

132. Carlson K, Kehle S, Meis L, Greer N, MacDonald R, Rutks I, Wilt TJ. VA Evidence-based Synthesis Program Reports. *The Assessment and Treatment of Individuals with History of Traumatic Brain Injury and Post-Traumatic Stress Disorder: A Systematic Review of the Evidence*. Washington (DC): Department of Veterans Affairs (US), 2009.

133. Dolan S, Martindale S, Robinson J, Kimbrel NA, Meyer EC, Kruse MI, Morissette SB, Young KA, Gulliver SB. Neuropsychological sequelae of PTSD and TBI following war deployment among OEF/OIF veterans. *Neuropsychology Review* 2012;22(1):21-34.

134. Veterans Health Administration. Screening and evaluation of traumatic brain injury (TBI) in Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) Veterans. 2017;VHA Directive 1184.

135. Prins A, Ouimette P, Kimerling R, Cameron RP, Hugelshofer DS, Shaw-Hegwer J, Thraikill A, Gusman FD, Sheikh JI. The primary care PTSD screen (PC-PTSD): Development and operating characteristics. *Primary Care Psychiatry* 2003;9(1):9-14.

136. Newman CW, Weinstein BE, Jacobson GP, Hug GA. The Hearing Handicap Inventory for Adults: Psychometric Adequacy and Audiometric Correlates. *Ear and Hearing* 1990;11(6):430-433.

137. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology* 1999;10(1):37-48.

138. Hernán MA, Hernández-Díaz S, Werler MM, Mitchell AA. Causal knowledge as a prerequisite for confounding evaluation: an application to birth defects epidemiology. *American Journal of Epidemiology* 2002;155(2):176-84.

139. Boyd RW, Lindo EG, Weeks LD, McLemore MR. On racism: A new standard for publishing on racial health inequities. *Health Affairs Blog*. Vol. 2020. Health Affairs, 2020.

140. VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. *Annals of Internal Medicine* 2017;167(4):268-274.

141. Hafeman DM, Schwartz S. Opening the Black Box: a motivation for the assessment of mediation. *International Journal of Epidemiology* 2009;38(3):838-45.

142. Petersen ML, Sinisi SE, van der Laan MJ. Estimation of direct causal effects. *Epidemiology* 2006;17(3):276-84.

143. Ananth CV, VanderWeele TJ. Placental abruption and perinatal mortality with preterm delivery as a mediator: disentangling direct and indirect effects. *American Journal of Epidemiology* 2011;174(1):99-108.

144. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *American Journal of Epidemiology* 2005;162(3):199-200.

145. Valeri L, Vanderweele TJ. Mediation analysis allowing for exposure-mediator interactions and causal interpretation: theoretical assumptions and implementation with SAS and SPSS macros. *Psychological Methods* 2013;18(2):137-50.

146. VanderWeele TJ. A unification of mediation and interaction: a 4-way decomposition. *Epidemiology* 2014;25(5):749-61.

147. Fox MP, Edwards JK, Platt R, Balzer LB. The critical importance of asking good questions: The role of epidemiology doctoral training programs. *American Journal of Epidemiology* 2019.

148. Westreich D, Edwards JK, Lesko CR, Stuart E, Cole SR. Transportability of Trial Results Using Inverse Odds of Sampling Weights. *American Journal of Epidemiology* 2017;186(8):1010-1014.

149. Textor J, van der Zander B, Gilthorpe MK, Liskiewicz M, Ellison GTH. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *International Journal of Epidemiology* 2016;45(6):1887-1894.

Appendix A. Institutional Review Board Documentation

Appendix A.1. ACOS Intial Review Approval and Institutional Review Board Exemption Approval and for “Hearing loss prevalence among post-9/11 Veterans using VA health care”

VA Portland Health Care System
Portland, OR

ACOS Notification - Initial Review

Date:	December 2, 2019
From:	David M. Cohen, M.D. ACOS/R&D
Investigator:	Kathleen Carlson, M.S., Ph.D.
Protocol:	Hearing loss prevalence among post-9/11 Veterans using VA health care
ID:	04554 Prom#: N/A Protocol#: N/A

DAVID M COHEN 386526
Digitally signed by DAVID M COHEN 386526
Date: 2019.12.06 11:18:03 -08'00'

I am pleased to inform you that the R&D Committee has conducted an initial review of this research protocol and granted initial approval to your study. This approval will expire on 12/01/2020.

VHA regulations mandate R&D review prior to submission of all forms of presentations (such as manuscripts, meeting abstracts, seminars, reviews, book chapters) arising from work on this project. VHA regulations also mandate that you inform the R&D Office immediately upon notification of acceptance. You are responsible for adhering to this requirement. Additional details can be found in the Presentation and Publication policy (under PI Services on the R&D web site).

As a reminder, all research records must be securely stored until their applicable disposition date, as per the disposition instructions approved by the National Archives and Records Administration (NARA) and published in VHA's Records Control Schedule (RCS) 10-1. This includes all research field facility records, including investigator's records and committee and subcommittee review records for basic, animal and human research.

Please retain this memo as an official document in your study files.

Research & Development Committee
VA Portland Health Care System
Portland, OR

APPROVAL - Initial Review (Subcommittee)

Date: December 2, 2019
From: Danielle Beaudry, R&D Committee Coordinator
Investigator: Kathleen Carlson, MS, PhD
Protocol: Hearing loss prevalence among post-9/11 Veterans using VA health care
Sponsor: 0000 = None • Admin: 01 = None
ID: 04554 Prom#: N/A Protocol#: N/A

The following items were reviewed and approved through Expedited Review:

- Abstract (10/28/2019; 10/31/2019 rcvd)
- Exemption from IRB Review (11/12/2019; 11/12/2019 rcvd)
- Variable list (10/28/2019; 10/31/2019 rcvd)
- Protocol (11/12/2019; 11/12/2019 rcvd)
- Scope of Work - IRQ Appendix L - Garnett McMillan (11/12/2019; 11/21/2019 rcvd)
- Scope of Work - IRQ Appendix L - James Henry (11/12/2019; 11/21/2019 rcvd)
- Scope of Work - IRQ Appendix L - Kathleen Carlson (11/12/2019; 11/21/2019 rcvd)
- Scope of Work - IRQ Appendix L - Kelly Reavis (11/12/2019; 11/21/2019 rcvd)
- Scope of Work - IRQ Appendix L - Tess Gilbert (11/12/2019; 11/21/2019 rcvd)

Expedited Approval was granted on 12/02/2019 for a period of 12 months and will expire on 12/01/2020. The reviewer was Travis Lovejoy, PhD. Your Continuing Review is scheduled for 11/02/2020. This Expedited review will be reported to the fully convened Research & Development Committee on 12/02/2019.

EXEMPTION APPROVAL

Alissa Hooper 1627025 Digitally signed by Alissa Hooper 1627025 Date: 2019.11.22 08:10:41 -08'00'

Date: November 22, 2019
From: Alissa Hooper, CIP
Investigator: Kathleen Carlson, MS, PhD
Protocol: Hearing loss prevalence among post-9/11 Veterans using VA health care
ID: 04554 Prom#: N/A Protocol#: N/A

The following items were reviewed and determined to be exempt from IRB review:

- Abstract (10/28/2019; 10/31/2019 rcvd)
- Exemption from IRB Review (11/12/2019; 11/12/2019 rcvd)
- Variable list (10/28/2019; 10/31/2019 rcvd)
- Protocol (11/12/2019; 11/12/2019 rcvd)
- Scope of Work - IRQ Appendix L - Garnett McMillan (11/12/2019; 11/21/2019 rcvd)
- Scope of Work - IRQ Appendix L - James Henry (11/12/2019; 11/21/2019 rcvd)
- Scope of Work - IRQ Appendix L - Kathleen Carlson (11/12/2019; 11/21/2019 rcvd)
- Scope of Work - IRQ Appendix L - Kelly Reavis (11/12/2019; 11/21/2019 rcvd)
- Scope of Work - IRQ Appendix L - Tess Gilbert (11/12/2019; 11/21/2019 rcvd)

Reviewer: Deniz Erten-Lyons, M.D.

Exemption from IRB review was granted on 11/22/2019. This exemption from IRB review will be reported to the fully convened IRB on 12/04/2019.

PLEASE NOTE: The PI is reminded that, if any changes are to be made to the project, the changes must be reviewed by the IRB Co-Chair (or designee) in order to assure that the project continues to meet the criteria for exemption from IRB review.

A waiver of authorization (45 CFR 164.512(i)) has been granted for use with this protocol. This waiver was reviewed and approved under expedited review procedures (38 CFR 16.110). The approval is granted based on the IRB-Co-Chair's determinations, as documented by their signature on the study's certificate of exemption, which includes HIPAA authorization waiver information sufficient to satisfy the following criteria:
•the research involves no more than minimal risk to the subjects and their privacy;
•the research involves using identifiable private information and, the research could not practicably be carried out without using such information in an identifiable format;
•the investigator's plan to destroy the identifiers at the earliest opportunity, consistent with the regulations, is adequate;

•the investigator has provided adequate written assurance that the protected health information (PHI) used will not be reused or disclosed outside the VHA (except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted);
•the request for the waiver of authorization includes a summary of the PHI to be used or disclosed; and
•the research could not be practicably conducted without this waiver of authorization and without access to and use of the PHI.

The PHI that may be used or disclosed for this study is limited to the health information indicated in the study protocol and the following identifiers: names from VADIR and CDW, may be verified within CPRS; street address, city, county and zip code when available from VADIR and CDW, may be verified within CPRS; birthdates and dates associated with military service from VADIR and CDW; audiogram dates and general medical encounter dates from CDW, may be verified with CPRS; social security numbers to link VADIR and CDW data.

Appendix A.2. Institutional Review Board Appoval for "Noise Outcomes in Service Members Epidemiology Study"

OREGON HEALTH & SCIENCE UNIVERSITY

IRB MEMO

OHSU Research Integrity Office
3181 SW Sam Jackson Park Road - L106RI
Portland, OR 97239-3098
(503)494-7887 irb@ohsu.edu

VA Research and Development Service
3710 SW U.S. Veterans Hospital Road - R&D
Portland, OR 97239-2999
(503)273-5152 pvamc-irb@va.gov

APPROVAL OF SUBMISSION

January 9, 2020

James Henry

503-220-8262 ext 57466
james.henry@va.gov

Heather M Belding 502048 Digitally signed by Heather M Belding 502048 Date: 2020.01.09 11:07:01 -08'00'

Dear James Henry:

On 1/9/2020, the IRB reviewed the following submission:

Type of Review:	Modification and Continuing Review, Study Closure or Check-in
Title of Study:	VAPORHCS / OHSU J: The Effect of Military Noise Exposure on Tinnitus and its Outcomes in Recently Discharged Veterans Seeking VA Health Care
Principal Investigator:	James Henry
IRB ID:	MODCR00012415
Funding:	Name: U.S. Army Medical Research and Materiel Command DOD, Grant Office ID: 9009223, Funding Source ID: PR121146; Name: U.S. Army Medical Research and Materiel Command DOD, Grant Office ID: 1009576
IND, IDE, or HDE:	None

Appendix A.3. Data use agreement within VAPORHCS - Agreement for the exchange of VA data within the VA Portland Health Care Systeem Between James Henry (IRB#3542) and Kathleen Carlson (IRB#4554)

DATA USE AGREEMENT WITHIN THE VAPORHCS

AGREEMENT FOR THE EXCHANGE OF VA DATA
WITHIN THE VA PORTLAND HEALTH CARE SYSTEM
BETWEEN James Henry (IRB#3542) AND Kathleen Carlson (IRB#4554)

Purpose:
This Agreement establishes the terms and conditions under which the VA Portland Health Care System (VAPORHCS), James Henry will provide, and Kathleen Carlson will use de-identified data.

References and Authorities:
- The Privacy Act of 1974, 5 U.S.C. § 552a, as amended
- The Health Insurance Portability and Accountability Act of 1994, Pub. L. 104-191
- Standards for Privacy of Individually Identifiable Health Information and Security Standards for the Protection of Electronic Protected Health Information (HIPAA Privacy and HIPAA Security Rules), 45 C. F. R. §§ 160, 164.
- Federal Information Processing Standards (FIPS) Publication 140-2, "Security Requirements for Cryptographic Modules," May 25, 2001
- The HITECH Act, Pub. L. 109-1

Terms of this Agreement:
1. This Agreement is by and between the VAPORHCS, James Henry (hereinafter referred to as the "Sender") and Kathleen Carlson (hereinafter referred to as the "Recipient").

2. This Agreement supersedes any and all agreements between the parties with respect to the transfer and use of data for the purpose described in this Agreement, and pre-empts and overrides any instructions, directions, agreements, or other understanding in or pertaining to any other prior communication with respect to the data and activities covered by this Agreement.

3. The Sender will transfer to the Recipient, through direct transfer of electronic data from the data repository folder to the study folder by personnel with access to both (Kathleen Carlson) or by other VA-approved transfer method, any and all related data for: Hearing loss prevalence among post-9/11 Veterans using VA health care (IRB# 4554). The following data will be sent: among Veterans only, service branch/component history, length of time between service separation date (or DD-214 form) and baseline exam, history of VA hearing test, sex, age, and audiometric data.

4. The type of Data being released include:
    a. ☐ Identified (i.e., names, addresses, dates, etc)
    b. ☐ Coded (i.e., direct identifiers removed, study code/ID included, etc)
    c. ☒ De-Identified (all 18 HIPAA identifiers and study code/ID removed)
        i. ☐ Verified Statistically; OR
        ii. ☒ Verified by Removal of 18 HIPAA identifiers and study code/ID

d. ☐ Limited Data Set[1]
e. ☐ Other: Explain

5. The following named individuals are designated as VAPORHCS's Points of Contact for performance of the terms of the Agreement.

Point-of-contact on behalf of VA Portland Health Care System

Privacy Officers: Phillip Cauthers x 56480 and Brooke Smith x 59602

Information Security Officer: Scott Griffin x 51369

6. Recipient agrees that the data provided (hereinafter referred to as the "Data") will be used solely for the purpose of Hearing loss prevalence among post-9/11 Veterans using VA health care (IRB# 4554).

7. Recipient is designated as custodian of this Data and will be responsible for the observance of all conditions of use and for establishment and maintenance of appropriate administrative, technical and physical security safeguards to prevent unauthorized use and to protect the confidentiality of the Data. If the custodianship is transferred within the organization the Recipient agrees to notify the Sender within (15) days of any change.

8. In addition to the Recipient's access, the following individuals and/or entities will also have access to or use the Data as required by the protocol (attach another sheet if additional space is needed):

Name	Title	Location
James Henry	Co-I	VAPORHCS-NCRAR
Garnet McMillan	Co-I	VAPORHCS-NCRAR
Kelly Reavis	Research Audiologist/ Data Analyst	VAPORHCS-NCRAR
Tess Gilbert	Program Manager	VAPORHCS-CIVIC

9. Access to the Data shall be restricted to authorized personnel only. Such personnel shall be advised of: (1) the confidential nature of the information; (2) safeguards required to protect the information; and (3) the administrative, civil and criminal penalties for noncompliance contained in applicable Federal laws. The Recipient agrees to limit access

[1] A Limited Data Set is protected health information from which certain specified direct identifiers of the individuals and their relatives, household members, and employers have been removed. These identifiers include name, address (other than town or city, state, or zip code), phone number, fax number, e-mail address, Social Security Number (SSN), medical record number, health plan number, account number, certificate and/or license numbers, vehicle identification, device identifiers, web universal resource locators (URL), internet protocol (IP) address numbers, biometric identifiers, and full-face photographic images. A limited data set is not de-identified information or data. A limited data set can only contain elements of dates (e.g., date of visit/encounter, birth/death, admission/discharge, etc.), certain geographic information (city, state, zip code), and other numbers, characteristics, or codes not listed as direct identifiers.

to, disclosure of and use of all Data provided under this Agreement. The Recipient agrees that access to the Data covered by this Agreement shall be limited to the minimum number of individuals who need access to the Data to perform the work described in this Agreement.

10. A number of VA directives exist to instruct employees on the proper handling of confidential and Privacy-protected Data. These include, but are not limited to, VA Handbook 5011/5, Chapter 4, (Alternative Workplace Arrangements), Security Guideline for Single-User Remote Access, Revision 3.0, VA Directive 6500, "Information Security Program," VA Directive 6504, Restrictions on Transmission, Transportation and Use Of, and Access to VA Data Outside of VA Facilities and VA Directive and Handbook 6502, "Privacy Policy", VHA Directive 1605, VHA Directive 1605.01 and 1605.2, and VHA series 1200 Handbooks.

11. No effort will be made to re-identify Data that are de-identified, which includes unscrambling social security numbers to reveal the real social security numbers.

12. The Sender relinquishes all ownership rights and responsibilities to the original and derivative Data file(s) provided to the Recipient under this Agreement.

13. Upon completion of the Data transfer, the Sender relinquishes all ownership rights to the copy of the Data that was provided to the Recipient.

14. Maintenance, storage, security, and safeguards will be the responsibility of the Recipient upon completion of the Data transfer.

15. In the event that an employee, Recipient or other user of Data covered by this Agreement, loses confidential or Privacy-protected Data or the Data is stolen or removed from designated locations or used or disclosed for purposes other than outlined in this Agreement, the employee or Recipient must report the incident immediately upon discovery of the incident to the VAPORHCS ISO, Privacy Officer, to the employee's or Recipient's immediate supervisor, and to the Recipient of the Data. The Recipient must notify the Sender, it is then the responsibility of the Sender to notify the Institutional Review Board (IRB) having oversight responsibility for the repository in accordance with the repository SOP. Senior management should be informed immediately by the supervisor or the Sender, who will further inform those in the chain of command. The incidents must also be reported to the Data Breach Response Service (DBRS) within one hour of the report of the incident. The incidents should be reported to the DBRS via the Information Security Officer (ISO) or designee, and entered into the Privacy Security Event Tracking System (PSETS) by the Privacy Officer. The ISO will report to the US-CERT (Computer Emergency Readiness Team) the information regarding the incident reported to the DBRS and in PSETS within the hour timeframe. A distribution list (VHA REPORTS TO US-CERT) has been established for use by the ISO in reporting all incidents involving personally identifiable information via Exchange, and includes the key VHA representatives that need to be notified as well as the DBRS.

16. Failure to comply with VA policy and regulations pertaining to Cyber Security and safeguarding confidential and Privacy-protected Data may violate Federal law. Some of these laws carry civil and criminal penalties.

17. None of the VAPORHCS Data, any Data extracted or derived from this transfer, or other Data files provided by the VAPORHCS, will be released to any other organization or individual external to the VAPORHCS without approval of the Sender. In addition, the Recipient will not publish nor release any information that is derived from the file that could possibly be expected to permit deduction of a beneficiary's identity. Infractions will be subject to prosecution under federal law.

18. The VAPORHCS has the authority to release this Data based on:

a. ☒ Data are de-identified (direct identifiers and study code/ID are removed) and thus does not include protected health information (PHI), which renders the Data not protected by the Privacy Rule.

b. ☐ Data are delivered as a Limited Data Set as defined by the HIPAA Privacy Rule at 45 CFR § 164.514(e) and thus satisfies the obligations under the HIPAA Privacy Rule.

c. ☐ HIPAA waiver approved by the IRB and Data sharing meets the following:

   i. Under the HIPAA Privacy Rule: documented approval of waiver of authorization from the IRB of record or Privacy Board that includes the following elements:

      1. Statement identifying the IRB or Privacy Board and the date on which the authorization was approved.

      2. Statement that the IRB or Privacy Board has determined that the waiver of authorization satisfies the following criteria: (1) the use or disclosure of PHI involves no more than minimal risk to the privacy of the individuals under criteria specified in the Privacy Rule, and (2) the research could not be practicably be conducted without access to the PHI; and documents a brief description of the PHI for which use or access has been determined to be necessary by the IRB or Privacy Board in order to conduct the research.

      3. A statement that the alteration or waiver of authorization has been reviewed and approved under either normal or expedited review procedures.

      4. The documentation is signed by the chair or other member as designated by the chair of the IRB or Privacy Board, as applicable.

   ii. Under the Privacy Act: Approval of use of the Data for research by the VAPORHCS's IRB of record.

   iii. Under 38 USC 7332: Written assurance that the purpose for requesting the Data is to conduct scientific research and that no personnel involved in the study may identify, directly or indirectly, any individual patient or subject in any report of such research or otherwise disclose patient or subject identities in any manner.

19. The Recipient will ensure compliance with the terms and conditions of this Agreement. The VA or VHA may request verification of compliance. The terms of this Agreement can be changed only by a written modification to the Agreement by the agency signatories (or their designated representatives) to this Agreement or by the parties adopting a new agreement in place of this Agreement.

20. This Agreement may be terminated by either party at any time for any reason upon 30 days written notice. Upon such notice, the Sender will notify the Recipient to follow the disposition of the Data, if ownership was retained, as described in paragraph 13.

21. On behalf of both parties the undersigned individuals hereby attest that they are authorized to enter into this Agreement and agree to all the terms specified herein.

James A. Henry 512463 Digitally signed by James A. Henry 512463 Date: 2020.04.16 06:55:23 -07'00'

James Henry Date
Research Investigator
VA Portland Health Care System

Kathleen F Carlson 512113 Digitally signed by Kathleen F Carlson 512113 Date: 2020.04.16 13:08:00 -07'00'

Kathleen Carlson Date
Research Investigator
VA Portland Health Care System

DAVID M COHEN 386526 Digitally signed by DAVID M COHEN 386526 Date: 2020.04.28 13:49:44 -07'00'

David M. Cohen, M.D. Date
Associate Chief of Staff, Research Service
VA Portland Health Care System

Scott Griffin 182598 Digitally signed by Scott Griffin 182598 Date: 2020.05.06 07:01:34 -07'00'

Information System Security Officer Date
VA Portland Health Care System

Brooke E Smith 388735 Digitally signed by Brooke E Smith 388735 Date: 2020.05.05 17:25:03 -07'00'

DATA USE AGREEMENT WITHIN THE VAPORHCS

Privacy Officer Date
VA Portland Health Care System

Zandrew Covington 277615 Digitally signed by Zandrew Covington 277615 Date: 2020.05.06 07:34:26 -07'00'

Zandrew Covington Date
Area Manager- VA Portland
VA Portland Area Manager

Appendix B. Supplemental materials for "A Bayesian Approach to Estimating Prevalence of Hearing Loss in Post-9/11 Veterans using VA Health Care"

Appendix B.1. Methods

Appendix B.1.1. Data cleaning

Prevalence of hearing loss was determined using audiometric thresholds collected as part of a comprehensive audiologic evaluation. The VA clinical audiograms were not collected for research purposes and therefore could be incomplete or with errors. Since 500, 1000, 2000, and 4000 Hz were necessary to determine hearing loss severity, any audiogram that was missing more than one threshold at these frequencies in either ear (<2% of the sample) was excluded. An anomaly in the administrative data entry is the presence of characters including negative, positive, and asterisk symbols. Positive and asterisk symbols were deleted, and the value retained. Negative symbols were only associated with values between 0 and 10 and were thought to indicate negative hearing levels (most standard audiometers can test down to -10 dB HL) and remained as is. Next, any threshold value that was not a multiple of 5 (typical of audiometric testing step sizes) was rounded up to the nearest multiple of 5 based on the recorded value (i.e., a threshold entry of 18 dB HL would be recoded as 20 dB HL). In the case of high thresholds that may be at the output limits of the audiometer, often an audiologist will either enter 'CNT' for *could not test* or set the threshold value to the limit of the audiometer plus 1 dB. A standard value for 'no response' at the limits of the audiometer could not be applied across audiograms because the maximum output varies by frequency, audiometer, and calibration. Instead, CNT values were set to missing and values that were not a multiple of 5 were rounded up. For example, many audiologists will enter a value of 96 dB HL to indicate the Veteran did not respond to the limits of the audiometer with a maximum output of 95 dB. For the purposes of this analysis, that value was also rounded up to the nearest multiple of 5; in this case, a value of 100 dB HL would be used for inclusion in the PTA. Any threshold with an entry of 'DNT,' which indicates the audiologist *did not test* that particular frequency, was set to missing. The table below highlights the value corrections applied to the administrative data only. NOISE Study audiograms were collected for research purposes with data double entered and cross checked for errors.[106] NOISE Study participants with no response at the limits of the audiometer were set to the maximum output by frequency for inclusion in the PTA.

Another unique feature of the administrative audiometric data was the presence of multiple (repeat) audiograms conducted on the same day. Review of the audiometric data suggested that repeat audiograms were mostly entered when the examination required masking to obtain a true threshold value. Masking is the process of applying a narrow band of noise to the opposite non-test ear in an attempt to isolate the test ear. If the audiologist was concerned the test ear was receiving help from the non-test ear (known as cross-hearing), a masker would be applied, and the threshold reestablished. If any repeat audiograms were available, the retest was used rather than the original. If only selected frequencies were retested, then those thresholds from the retested frequencies were used in combination with the thresholds from the original audiogram.

Table B.1. Database repository hearing threshold entries, subsequent recode, and counts by audiometric test frequency.

Database Repository Entry (dB HL)	Recode (dB HL)	250	500	1000	2000	3000	4000	6000	8000	Total
+	.	1	1	1	1	0	0	1	4	9
+100	100	1	0	0	0	0	0	1	0	2
+105	105	0	4	4	5	5	7	8	11	44
+90	90	0	0	0	0	0	0	0	2	2
-0	0	0	2	1	1	3	0	0	1	8
-05	-5	0	13	6	27	21	17	11	23	118
-1	0	0	1	0	1	1	1	1	1	6
-10	-10	187	232	236	615	568	537	472	1540	4387
-10*	-10	0	0	0	0	0	0	0	1	1
-2	0	2	3	2	1	6	2	2	5	23
-3	0	0	0	0	0	1	0	0	0	1
-4	0	3	0	0	0	0	1	1	5	10
-5	-5	3520	5171	4689	10058	6644	5293	3866	9682	48923
-5*	-5	0	0	0	0	0	0	0	1	1
-6	-5	0	0	0	0	0	0	0	2	2
-8	-5	0	0	0	0	0	0	0	1	1
0	0	67105	81951	79009	102931	67216	54205	40927	77132	570476
0+	0	1	1	0	0	0	0	0	0	2
00	0	243	299	322	440	301	275	221	385	2486
000	0	0	0	1	0	0	0	1	1	3
0000000	0	1	0	0	0	0	0	0	0	1
000000000	0	0	0	0	0	1	0	0	0	1
0000000000000	0	0	0	0	1	0	0	0	0	1
000000000000000	0	1	0	0	0	0	0	0	0	1
01	5	6	2	2	2	3	0	1	0	16
010	10	1	0	0	0	1	1	1	4	8
0105+	105	0	0	0	0	0	0	0	2	2
015	15	1	1	0	0	0	1	3	4	10
02	5	2	4	1	1	1	0	0	1	10
020	20	1	0	0	0	0	0	0	0	1
03	5	0	0	0	0	1	1	0	0	2
04	5	1	1	1	1	0	0	0	0	4

040	40	0	0	0	0	0	1	0	0	1
05	5	1303	1458	1600	1533	1090	861	778	1026	9649
06	10	0	0	1	1	0	2	1	0	5
065	65	1	0	0	0	0	0	0	0	1
08	10	1	0	3	0	0	1	1	2	8
09	10	0	0	1	0	0	0	0	0	1
090	90	0	0	0	0	0	1	0	0	1
1	5	36	25	31	29	20	22	10	19	192
10	10	329503	336303	337921	273152	226104	202168	176389	188559	2070099
10+	10	2	0	0	0	1	0	0	4	7
11	15	3	1	3	3	3	3	2	2	20
12	15	50	66	66	47	52	43	37	43	404
13	15	6	3	5	1	4	2	3	1	25
14	15	67	62	58	62	60	57	44	51	461
15	15	266649	269594	265084	228004	206439	193863	183045	176089	1788767
15*	15	1	0	0	0	0	0	0	0	1
15+	15	2	0	0	0	0	0	0	4	6
16	20	68	75	66	66	47	55	42	62	481
17	20	2	7	5	5	1	3	5	2	30
18	20	50	63	81	62	47	53	33	34	423
19	20	15	14	9	12	8	7	7	7	79
2	5	21	29	28	22	30	24	21	18	193
20	20	152478	152536	153656	150591	147276	144420	147296	135549	1183802
20*	20	0	0	0	0	0	0	1	0	1
20+	20	0	0	1	0	0	0	0	1	2
20+*	20	0	0	0	0	0	0	1	0	1
21	25	2	6	2	6	6	4	1	5	32
22	25	52	78	67	53	40	44	40	31	405
23	25	6	8	6	6	3	7	1	0	37
24	25	53	50	83	61	46	54	48	39	434
25	25	81367	81410	84884	96006	104911	109121	113142	104419	775260
25*	25	0	1	0	0	0	0	0	0	1
25+	25	8	10	7	5	9	13	10	8	70
26	30	45	47	44	49	42	27	28	33	315
27	30	2	2	8	5	6	2	5	2	32
28	30	32	38	45	28	24	32	29	24	252

29	30	6	4	7	7	5	8	12	2	51
3	5	2	1	2	2	5	7	5	4	28
30	30	32459	35362	40899	53016	64160	68805	69898	62002	426601
30*	30	0	0	1	0	0	0	0	0	1
30+	30	1	1	0	0	0	0	0	0	2
31	35	0	3	2	4	1	3	3	5	21
32	35	13	15	22	19	27	32	23	19	170
33	35	1	1	0	3	0	7	2	1	15
34	35	16	13	17	19	25	33	21	19	163
35	35	19776	22133	26213	37131	50670	57756	57552	52305	323536
35*	35	1	0	0	1	0	1	0	0	3
35+	35	0	0	0	1	0	0	0	2	3
36	40	14	18	11	18	18	14	19	20	132
37	40	0	0	1	0	0	1	3	2	7
38	40	11	6	11	21	7	18	11	11	96
39	40	0	0	1	0	3	1	0	2	7
4	5	21	27	21	27	21	37	15	31	200
40	40	12761	14324	17739	26520	39894	49821	47057	44548	252664
40*	40	1	0	0	3	2	3	1	1	11
40+	40	0	2	2	2	0	0	0	1	7
41	45	0	0	0	2	0	3	0	0	5
42	45	2	10	11	10	10	11	11	16	81
43	45	0	0	0	0	0	0	4	0	4
44	45	5	3	9	8	6	20	11	11	73
45	45	8118	9351	12418	19504	33881	44194	40440	39341	207247
45*	45	1	3	4	1	7	11	0	7	34
46	50	2	5	3	7	5	18	10	12	62
47	50	0	0	1	0	1	0	1	3	6
48	50	1	0	2	5	9	7	8	9	41
49	50	0	1	0	0	2	1	0	1	5
5	5	224120	241095	244950	216854	162341	136965	109212	141052	1476589
5+	5	3	0	0	0	0	0	0	1	4
50	50	5793	6623	8998	15424	30960	41329	37405	37512	184044
50*	50	2	4	2	3	6	8	10	2	37
51	55	0	1	2	2	0	2	2	1	10
52	55	1	1	4	5	3	6	6	13	39

53	55	0	0	1	0	1	2	1	1	6
54	55	4	3	1	4	8	18	8	11	57
55	55	4235	4822	6349	12586	29061	39562	34956	36279	167850
55*	55	4	5	1	5	10	19	9	13	66
55+	55	1	0	0	0	0	0	0	1	2
56	60	1	1	5	1	11	16	5	5	45
57	60	0	0	0	0	2	0	0	0	2
58	60	1	0	1	6	5	5	13	6	37
6	10	36	28	35	32	26	27	33	40	257
60	60	3087	3452	4738	10364	25579	35878	33371	34470	150939
60*	60	3	3	6	4	9	10	5	8	48
60+	60	0	0	0	0	0	0	1	2	3
61	65	0	0	1	0	1	0	2	2	6
62	65	1	0	0	1	1	5	4	3	15
63	65	0	0	0	0	1	0	2	0	3
64	65	0	1	2	2	2	7	5	5	24
65	65	2062	2434	3417	7896	19901	30442	29566	30208	125926
65*	65	3	2	1	1	10	11	11	12	51
65+	65	1	1	0	0	0	0	0	1	3
66	70	0	0	0	3	3	5	6	7	24
67	70	0	0	0	0	0	1	0	1	2
68	70	0	0	0	1	1	1	4	1	8
69	70	0	0	0	2	0	1	0	0	3
7	10	3	3	1	2	0	2	0	2	13
70	70	1508	1727	2284	5401	14044	23011	23372	24692	96039
70*	70	2	1	2	5	10	20	10	9	59
70+	70	5	1	1	1	0	0	0	33	41
71	75	0	0	0	0	0	1	2	1	4
72	75	1	1	0	3	5	3	1	5	19
74	75	0	1	0	2	1	6	4	1	15
75	75	1040	1166	1651	3550	8864	15743	17469	19368	68851
75*	75	1	1	1	2	4	4	9	7	29
75+	75	0	1	0	1	0	1	1	61	65
76	80	0	1	0	1	0	2	2	2	8
78	80	0	0	2	1	0	2	4	3	12
79	80	0	0	0	0	0	1	1	0	2

8	10	41	32	39	41	19	27	19	38	256
80	80	692	870	1129	2220	5393	10295	12325	15030	47954
80*	80	2	4	2	5	0	5	4	11	33
80+	80	8	2	0	4	2	0	6	48	70
82	85	0	0	0	0	1	2	1	3	7
84	85	0	0	0	1	1	0	6	2	10
85	85	527	619	798	1261	3263	7101	9105	10290	32964
85*	85	2	1	1	1	5	4	7	5	26
85+	85	5	2	0	0	0	0	0	171	178
86	90	0	1	1	1	2	1	1	1	8
88	90	0	0	0	0	0	1	3	4	8
89	90	0	0	0	0	0	1	1	0	2
9	10	2	4	1	3	4	1	2	1	18
90	90	417	478	566	827	1941	4452	6681	7442	22804
90*	90	1	1	2	1	4	6	5	5	25
90+	90	44	15	9	5	3	7	14	2368	2465
90+*	90	0	0	0	0	0	0	0	4	4
91	95	0	0	0	0	0	1	0	0	1
92	95	0	1	0	0	1	1	2	0	5
94	95	0	0	0	0	0	1	0	1	2
95	95	276	384	386	536	1199	2794	4152	3846	13573
95*	95	0	1	3	2	1	3	1	4	15
95+	95	41	13	4	3	2	8	40	1437	1548
96	100	0	0	0	0	0	2	1	2	5
96+	100	0	0	0	0	0	0	0	1	1
98	100	0	0	0	0	1	1	1	0	3
99	100	0	0	0	1	0	0	0	0	1
100	100	268	271	326	395	813	1900	2803	2174	8950
100*	100	0	0	0	2	1	2	3	4	12
100+	100	210	99	94	94	110	152	819	1016	2594
100+*	100	1	0	0	0	0	0	0	1	2
101	100	3	0	0	0	0	0	0	1	4
103	100	1	0	0	0	0	0	0	1	2
104	100	0	0	0	0	0	0	1	0	1
104+	100	0	0	0	0	1	1	1	1	4
105	105	176	242	267	354	603	1182	1584	885	5293

105*	105	0	1	0	0	1	0	2	2	6
105+	105	649	1016	1213	1543	1864	2813	2878	2681	14657
105+*	105	1	2	2	2	1	1	3	1	13
110	110	0	1	3	3	4	6	8	3	28
110*	110	0	0	0	1	1	1	3	0	6
110+	110	1	4	3	2	2	5	7	6	30
110+*	110	0	0	0	1	1	1	0	1	4
CNT	.	426	463	485	450	433	459	428	484	3628
DNT	.	153	84	123	80	67	88	67	108	770

Abbreviations: CNT, could not test; DNT, did not test

Appendix C. Supplemental materials for "Occupational Noise Exposure and Longitudinal Hearing Changes in US Military Personnel"

Appendix C.1. Methods

Appendix C.1.1. Description of statistical analysis

The unit of analysis is the audiogram. Let $\underline{y_i}$ denote the i^{th} observed audiogram, i=1…2597, composed of pure tone thresholds elicited at 0.5, 1, 2, 3, 4, and 6 kHz in 490 Service Member ears. We assume a multivariate normal model for the audiograms $\underline{y_i} \sim N_6\left(\underline{\mu_i}, \Sigma\right)$, with $\underline{\mu_i} = \{\mu_i^{0.5}, \mu_i^1, \mu_i^2, \mu_i^3, \mu_i^4, \mu_i^6\}^T$. Σ is given a first-order autoregressive structure with heterogenous variances, denoted ARH(1), such that

$$\Sigma = \begin{pmatrix} \sigma_{0.5}^2 & \sigma_{0.5}\sigma_1\rho & \sigma_{0.5}\sigma_2\rho^2 & \sigma_{0.5}\sigma_3\rho^3 & \sigma_{0.5}\sigma_4\rho^4 & \sigma_{0.5}\sigma_6\rho^5 \\ \sigma_{0.5}\sigma_1\rho & \sigma_1^2 & \sigma_1\sigma_2\rho & \sigma_1\sigma_3\rho^2 & \sigma_1\sigma_4\rho^3 & \sigma_1\sigma_6\rho^4 \\ \sigma_{0.5}\sigma_2\rho^2 & \sigma_1\sigma_2\rho & \sigma_2^2 & \sigma_2\sigma_3\rho & \sigma_2\sigma_4\rho^2 & \sigma_2\sigma_6\rho^3 \\ \sigma_{0.5}\sigma_3\rho^3 & \sigma_1\sigma_3\rho^2 & \sigma_2\sigma_3\rho & \sigma_3^2 & \sigma_3\sigma_4\rho & \sigma_3\sigma_6\rho^2 \\ \sigma_{0.5}\sigma_4\rho^4 & \sigma_1\sigma_4\rho^3 & \sigma_2\sigma_4\rho^2 & \sigma_3\sigma_4\rho & \sigma_4^2 & \sigma_4\sigma_6\rho \\ \sigma_{0.5}\sigma_6\rho^5 & \sigma_1\sigma_6\rho^4 & \sigma_2\sigma_6\rho^3 & \sigma_3\sigma_6\rho^2 & \sigma_4\sigma_6\rho & \sigma_6^2 \end{pmatrix}.$$

We define $\underline{\mu_i} = \underline{X}_i \cdot \underline{\beta} + \underline{\delta}_{S[i]} + 1_6 \cdot \theta_{SE[i]}$, where 1_6 is a column vector of ones. The bracket notation identifies the index attached to the i^{th} audiogram. For example, $S[i]$ identifies the S^{th} subject providing the i^{th} audiogram. $\underline{X}_i$ corresponds to the fixed effects in the model (see Table X). β is the fixed effects parameter vector. We also assume a multivariate normal model for the subject-specific random effects $\underline{\delta}_S \sim N_6(0, \tau)$, with $\underline{\delta}_S = \{\delta^{0.5}, \delta^1, \delta^2, \delta^3, \delta^4, \delta^6\}_S$ and where τ is ARH(1). $\theta_{SE[i]}$ is a random subject-ear effect that is constant across frequencies for the E^{th} ear of the S^{th} subject. Each i^{th} audiogram provides 6x70 matrix ($\underline{X}_i$) of covariates, one row per frequency, described in Table C.3. Elements are constant down rows, within columns, unless the column pertains to a stimulus frequency.

Table C.1. Distribution of the number of audiograms for 246 military personnel.

Number of Audiograms	n (%) of Military Personnel
1	7 (2.9)
2	19 (7.7)
3	32 (13.0)
4	44 (17.9)
5	37 (15.0)
6	34 (13.8)
7	31 (12.6)
8	16 (6.5)
9	15 (6.1)
10	3 (1.2)
11	2 (0.8)
12	1 (0.4)
13	2 (0.8)
14	1 (0.4)
15	1 (0.4)
17	1 (0.4)

Table C.2. Number of audiograms (cumulative percent) by year and service branch.

Year	Army[a] Number Audiograms (Cumulative %)	Air Force[b] Number Audiograms (Cumulative %)	Marine Corps[c] Number Audiograms (Cumulative %)	Navy[b] Number Audiograms (Cumulative %)
2001	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
2002	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.6)
2003	4 (0.2)	2 (1.2)	6 (2.3)	8 (3.2)
2004	22 (1.5)	4 (3.6)	10 (4.7)	10 (6.4)
2005	38 (3.8)	4 (6.0)	2 (5.1)	2 (7.0)
2006	64 (7.5)	2 (7.1)	12 (7.9)	12 (10.8)
2007	106 (13.7)	8 (11.9)	24 (13.5)	12 (14.7)
2008	120 (20.8)	12 (19.1)	22 (18.7)	20 (21.0)
2009	192 (32.0)	18 (29.8)	32 (26.1)	16 (26.1)
2010	234 (45.8)	20 (41.7)	32 (33.6)	38 (38.2)
2011	242 (60.0)	26 (57.1)	50 (45.2)	48 (53.5)
2012	216 (72.7)	21 (69.6)	94 (67.1)	37 (65.3)
2013	192 (83.9)	16 (79.2)	65 (82.3)	36 (76.8)
2014	121 (91.0)	16 (88.7)	50 (93.9)	39 (89.2)
2015	105 (97.2)	13 (96.4)	19 (98.4)	20 (95.6)
2016	44 (99.8)	4 (98.8)	7 (100.0)	14 (100)
2017	4 (100.0)	2 (100.0)	0 (100.0)	0 (100)
Total	1704 -	168 -	429 -	314 -

[a] Enforced population-level surveillance in 2006.
[b] Only enroll military personnel in the hearing conservation program who are deemed noise exposed.[69]
[c] Began population-level surveillance in 2012.

Table C.3. 6 x 70 matrix $(\underline{X}_i)$ of covariates[a]

Column	Description of Fixed Effect
1	1s for the intercept
2	Age
3	Service branch: 1 if Army, 0 otherwise
4	Service branch: 1 if Marine Corps, 0 otherwise
5	Service branch: 1 if Navy, 0 otherwise
6	Service branch: 1 if Air Force, 0 otherwise
7	Log_2 frequency
8	Log_2 frequency^2
9	2-way interaction: age *x* Log_2 frequency
10	2-way interaction: age *x* Log_2 frequency^2
11	Cumulative exposure to basic training
12	Cumulative exposure to an occupation with a low noise exposure rank
13	Cumulative exposure to an occupation with a moderate noise exposure rank
14	Cumulative exposure to an occupation with a high noise exposure rank
15	2-way interaction: cumulative exposure to basic training, Log_2 frequency
16	2-way interaction: cumulative exposure to basic training *x* Log_2 frequency^2
17	2-way interaction: cumulative exposure to basic training *x* Army
18	2-way interaction: cumulative exposure to basic training *x* Marine Corps
19	2-way interaction: cumulative exposure to basic training *x* Navy
20	2-way interaction: cumulative exposure to basic training *x* Air Force
21	3-way interaction: cumulative exposure to basic training *x* Army *x* Log_2 frequency
22	3-way interaction: cumulative exposure to basic training *x* Marine Corps *x* Log_2 frequency
23	3-way interaction: cumulative exposure to basic training *x* Navy *x* Log_2 frequency
24	3-way interaction: cumulative exposure to basic training *x* Air Force *x* Log_2 frequency

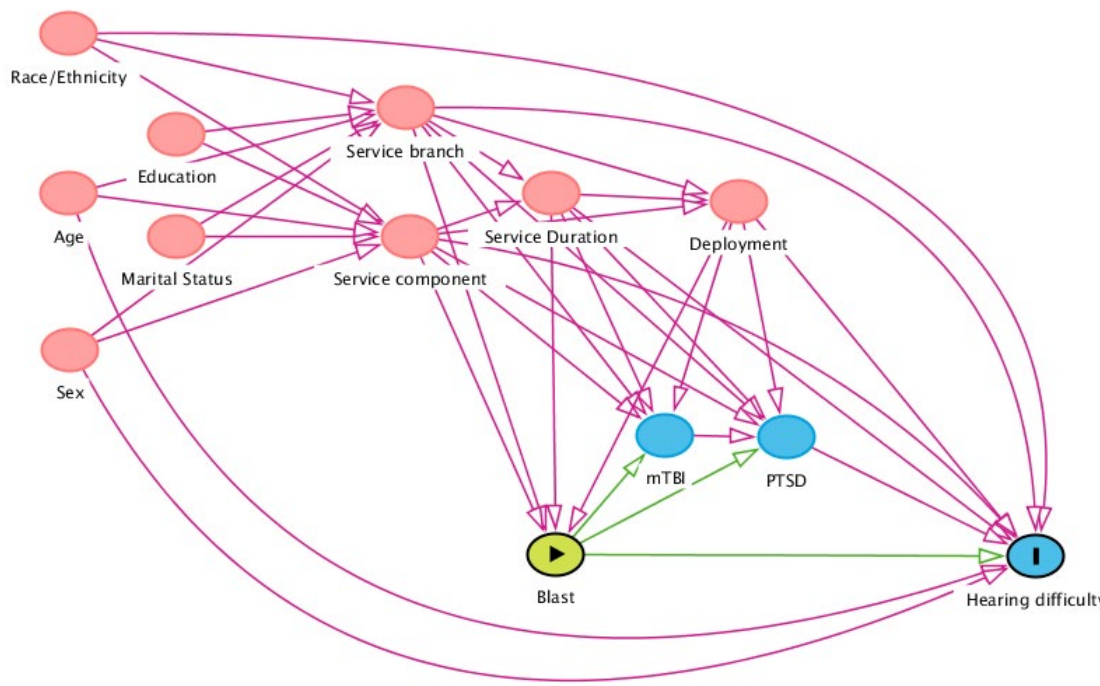
25	3-way interaction: cumulative exposure to basic training *x* Army *x* Log_2 $frequency^2$
26	3-way interaction: cumulative exposure to basic training *x* Marine Corps *x* Log_2 $frequency^2$
27	3-way interaction: cumulative exposure to basic training *x* Navy *x* Log_2 $frequency^2$
28	3-way interaction: cumulative exposure to basic training *x* Air Force *x* Log_2 $frequency^2$
29	2-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Log_2 frequency
30	2-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Log_2 $frequency^2$
31	2-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Army
32	2-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Marine Corps
33	2-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Navy
34	2-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Air Force
35	3-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Army *x* Log_2 frequency
36	3-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Marine Corps *x* Log_2 frequency
37	3-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Navy *x* Log_2 frequency
38	3-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Air Force *x* Log_2 frequency
39	3-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Army *x* Log_2 $frequency^2$
40	3-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Marine Corps *x* Log_2 $frequency^2$
41	3-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Navy *x* Log_2 $frequency^2$
42	3-way interaction: cumulative exposure to an occupation with a low noise exposure rank *x* Air Force *x* Log_2 $frequency^2$
43	2-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Log_2 frequency
44	2-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Log_2 $frequency^2$
45	2-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Army
46	2-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Marine Corps
47	2-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Navy
48	2-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Air Force
49	3-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Army *x* Log_2 frequency
50	3-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Marine Corps *x* Log_2 frequency

51	3-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Navy *x* Log_2 frequency
52	3-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Air Force *x* Log_2 frequency
53	3-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Army *x* Log_2 frequency^2
54	3-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Marine Corps *x* Log_2 frequency^2
55	3-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Navy *x* Log_2 frequency^2
56	3-way interaction: cumulative exposure to an occupation with a moderate noise exposure rank *x* Air Force *x* Log_2 frequency^2
57	2-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Log_2 frequency
58	2-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Log_2 frequency^2
59	2-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Army
60	2-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Marine Corps
61	2-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Navy
62	2-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Air Force
63	3-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Army *x* Log_2 frequency
64	3-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Marine Corps *x* Log_2 frequency
65	3-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Navy *x* Log_2 frequency
66	3-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Air Force *x* Log_2 frequency
67	3-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Army *x* Log_2 frequency^2
68	3-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Marine Corps *x* Log_2 frequency^2
69	3-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Navy *x* Log_2 frequency^2
70	3-way interaction: cumulative exposure to an occupation with a high noise exposure rank *x* Air Force *x* Log_2 frequency^2

[a]Each i^{th} audiogram provides 6x70 matrix ($\underline{X}_i$) of covariates, one row per frequency. Elements are constant down rows, within columns, unless the column pertains to a stimulus frequency.

Appendix D. Supplemental materials for "Blast Exposure and Self-Reported Hearing Difficulty in Normal Hearing Service Members and Veterans: The Mediating Role of Post-Traumatic Stress Disorder"

Figure D.1. Directed acyclic graph[a] depicting theorized causal pathways between blast exposure and self-reported hearing difficulty with mediation by PTSD.[149]



[a]Some arrows have been omitted to increase clarity of the causal effects of interest.

Table D.1. E-values[a] for the point estimate and lower confidence interval for the fully adjusted regression models and causal mediation model.

	E-Value for Point Estimate	E-Value for Lower Confidence Interval
Fully Adjusted Regression Models		
Blast → Hearing difficulty	3.41	1.92
Blast → PTSD	3.00	1.92
PTSD → Hearing difficulty	5.65	3.82
Causal Mediation Model		
Total Effect	3.82	2.15
Natural Direct Effect	2.79	1.43
Natural Indirect Effect	1.92	1.00

Abbreviations: PTSD, post-traumatic stress disorder
[a]E-value represents the strength of an unmeasured confounder necessary to suggest a reasonable alternative explanation for the observed associations.[140]