To see the TOC, open the View tab above and under the Show section check the box for Navigation Pane.

Please contact Claire if you have content to add!

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**Medical Treatise Evidence Index**

*When discussing medical treatise evidence, highlight any research that shows statistical likelihoods of developing the secondary disability and any other indications that other possible causes of the secondary condition can be ruled out. The stronger the evidence that rules out other causes, the better because under applicable caselaw that makes treatise evidence sufficient to prove a nexus.*

# Boilerplate Explanation That Treatise Evidence is Sufficient

*[use this boilerplate after a discussion of medical literature supporting service connection to explain why the pro-claimant standard of review warrants service connection even without scientific certainty]*

Although the relationship between COPD and OSA might not be fullyunderstood, there is enough medical literature and evidence in this particular case to warrant secondary service connection. After all, service connection does not require scientific certainty about the mechanism of causation—rather, the claimed condition need be only at least as likely as not related to the primary, service-connected disability. Further, VA must grant a claimant service connection when the positive and negative evidence is “nearly equal” or in “approximate balance.” *Lynch v. McDonough*, 999 F.3d 1391, 1394 (Fed. Cir. 2021).

Moreover, the Court of Appeals for Veterans Claims has indicated that “medical article or treatise evidence, standing alone,” is sufficient to establish a causal relationship for service connection if it “discusses generic relationships with a degree of certainty such that, under the facts of a specific case, there is at least plausible causality based upon objective facts rather than on an unsubstantiated lay medical opinion.” *See Sacks v. West*, 11 Vet. App. 314, 317 (1998) (stating its holding that treatise evidence was insufficient did not extend to cases with treatise evidence showing degree of certainty). VA must not impose too high a burden on the Veteran, particularly in this case where the medical literature is not merely a speculative discussion of association without causation—but rather puts forth supported theories of causation consistent with the Veteran’s contentions.

The medical articles and other evidence here raise a plausible causal connection supported by science—and although there might be alternative explanations, those explanations are no more likely than the one that supports service connection in this case. In other words, the literature and evidence show that the claimed condition was ***at least as likely as not caused or aggravated by the Veteran’s service-connected COPD***.

VA must not deny the claim based on an inadequate medical opinion that ignores the plausible and statistically likely connection proven by the medical evidence cited here. In addition, a medical opinion is inadequate if discounts the scientific evidence suggesting a causal relationship without explaining what other possible factors are more likely to have caused the current disability. Without engaging in a comparative analysis of risk factors, it is impossible for a clinician to opine that any cause is less or as likely as any other.

# Musculoskeletal

#### Musculoskeletal Disability Causes Additional Musculoskeletal Disability

The musculoskeletal system can be understood as a complex network of parts in which injuries “in one part of the body are known to affect other muscle groups.” Andrew C. Murphy et al., *Structure, Function, & Control of the Human Musculoskeletal Network*, 16 PLoS Biol. (2018) (enclosed).

#### Obesity Causes Gout

* + New medical literature, Tongjun Mao et al., *Relationship Between Gout, Hyperuricemia, and Obesity*, 16 Diabetology & Metabolic Synd. 24 (2024), available at <https://dmsjournal.biomedcentral.com/articles/10.1186/s13098-024-01268-1>, is relevant to show “higher body mass index (BMI) has been consistently linked to an elevated risk of hyperuricemia and gout, while weight loss has been shown to reduce the likelihood of developing gout” and delineating plausible mechanisms for causation including heightened adiposity contributing “to an augmented overall nucleic acid metabolism, subsequently fostering uric acid synthesis through purine metabolism” and that “obesity may induce aberrations in glomerular hemodynamics and provoke the overactivation of the renin-angiotensin-aldosterone system, potentially leading to obesity-associated nephropathy.” “Insulin resistance, a common consequence of obesity, can further complicate urate metabolism by influencing the renal excretion of uric acid.”

#### Obesity Causes Musculoskeletal Disability

Finally, the Veteran also contends entitlement to service connection for musculoskeletal disability secondary to obesity caused by weight gain due to service-connected and claimed disabilities. The new and relevant lay statement explains how the Veteran’s service-related disabilities have caused weight gain. Obesity and overweight are shown to be significant factors in the development and progression of musculoskeletal disability such as low back pain (Tom Ivar Lund Nilsen et al., *Physical Exercise, Body Mass Index, and Risk of Chronic Pain in the Low Back and Neck/Shoulders: Longitudinal Data from the Nord-Trøndelag Health Study*, 174 Am. J. Epid. 267 (2011), available at <https://pubmed.ncbi.nlm.nih.gov/21633119/> (enclosed)); and osteoarthritis generally (Lauren K. King et al., *Obesity & Osteoarthritis*, 138 Indian. J. Med. Res. 185 (2013), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3788203/> (enclosed)).

* Nexus to service-connected disabilities through obesity:
  + New medical literature, Lauren K. King et al., *Obesity & Osteoarthritis*, 138 Indian. J. Med. Res. 185 (2013), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3788203/>, is relevant to show that obesity and overweight are risk factors for osteoarthritis.

#### Unreported/Minor Musculoskeletal Injury Predicts Future Disability

First, research shows that musculoskeletal injury is common, but servicemembers tend to underreport these injuries during service, instead opting to self-treat these conditions. Laurel Smith et al., *Underreporting of Musculoskeletal Injuries in the US Army: Findings from an Infantry Brigade Combat Team Survey Study*, 8 Sports Health 507 (2016), available at <https://‌pubmed.‌ncbi.nlm.nih.gov/‌27789871/> (enclosed). A 2016 survey study of 1388 soldiers in an infantry brigade reported an alarming number of musculoskeletal injuries across all military occupation specialties (infantry, armor, field artillery, engineers, medics, mechanics, and so on). *Id.* at 508–09. They reported a total of 3202 musculoskeletal injuries over the previous 12-month period—only 51 percent of which had been reported. *Id.* at 509. The soldiers gave various reasons for their choice not to report nearly half of their injuries: fear of loss of career opportunities, avoidance of negative perceptions, avoiding profiles (preventing them from working), negative experiences with healthcare providers, and inconvenience were listed among the top reasons. *Id.* This scientific evidence thus lends additional credibility to the Veteran’s reports of in-service injury and pain, even though it went unrecorded.

In addition, the Department of Defense itself acknowledges the likelihood of musculoskeletal injury during typical circumstances of service. An Army fact sheet informs soldiers that load-carriage activities associated with Army training “puts repeated stress on the body’s skin, bones, muscles, and nerves and can cause numerous injuries” most commonly including “[k]nee pain and various musculoskeletal knee injuries[,] [b]ack pain, strains, and other lower and upper back injuries,” foot injuries such as metatarsalgia, and ankle injuries. *Foot Marching and Load-Carriage Injuries*, Army Public Health Center (Provisional) – Injury Prevention Program, Fact Sheet 12-008-0416 (enclosed). The Army acknowledges that, although behavior modification may reduce the chance or severity of injuries, “some factors cannot be changed.” *Id.*

This research thus provides a statistical basis for the credibility of the Veteran’s reports in this case, despite any choice not to report continuous symptoms of injury during his service.

Second, medical research proves that musculoskeletal injuries during service—even if minor enough not to require continuous treatment at the time—can lead to reinjury and progression in the future. “Early recurrences represent the most frequent complications of muscle injuries; incidence of repeat injury has been reported to be approximately 30%.” F. Alessandrino and G. Balconi, *Complications of Muscle Injuries*, 16 J. Ultrasound 215 (2013), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC3846951/> (enclosed). Further, “injured muscle is more atrophic than the healthy, uninjured muscle,” which also increases the risk of delayed recurrences of muscle injury. *Id.* at 220.

The same is true of joint injuries; osteoarthritis, for example, is considered a “wear and tear” disease, the risk for which is increased by history of joint injuries and repeated stress on the joint. *Osteoarthritis*, Mayo Clinic, <https://www.mayoclinic.org/diseases-conditions/‌osteoarthritis/‌symptoms-causes/‌syc-20351925> (May 8, 2019) (enclosed). And with respect to military-related back injuries in particular, research has shown that “a history of suffering from [low back pain] seems to predict a later [low back pain] episode.” Ville M. Mattila et al., *Low Back Pain During Military Service Predicts Low Back Pain Later in Life*, 12 PLoS ONE (Mar. 2017) (enclosed).

This new and relevant evidence shows that even injuries that may seem minor enough to go unreported at the time can progress into debilitating conditions later in life.

#### Unreported – RO Version

* Current disability:
  + New self-report of symptoms form shows persistent symptoms of disability.
* In-service event, injury, or disease:
  + New self-report of symptoms form shows injury and onset during service.
  + New U.S. Army evidence, *Foot Marching and Load-Carriage Injuries*, Army Public Health Center (Provisional) – Injury Prevention Program, Fact Sheet 12-008-0416, is relevant to show that the types of injuries sustained by the Veteran are highly common among servicemembers due to the typical strenuous activities under the normal circumstances of service.
  + New medical article, Laurel Smith et al., *Underreporting of Musculoskeletal Injuries in the US Army: Findings from an Infantry Brigade Combat Team Survey Study*, 8 Sports Health 507 (2016), available at <https://‌pubmed.‌ncbi.nlm.nih.gov/‌27789871/>, is relevant to show that many musculoskeletal injuries and complaints go unreported among servicemembers. This bolster’s the Veteran’s statements of in-service onset despite a lack of treatment records.
* Nexus:
  + New self-report of symptoms form shows continued symptoms since service.

VA’s M21-1 Adjudication Procedures Manual acknowledges: “For any disability shown to be chronic in a medical sense, but not listed in 38 C.F.R. 3.309(a), continuous symptoms ***[not treatment]*** may be used to satisfy the nexus element for direct SC under 38 C.F.R. 3.303(a). When the nexus element is met, ***a medical opinion is not needed.***” M21-1 V.ii.2.A.1.c (emphasis and alteration added).

* + New medical article, F. Alessandrino and G. Balconi, *Complications of Muscle Injuries*, 16 J. Ultrasound 215 (2013), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC3846951/>, is relevant to show that injuries during service—even if minor enough not to require continuous treatment at the time—can lead to reinjury and progression in the future.
  + New medical article, *Osteoarthritis*, Mayo Clinic, <https://www.mayoclinic.org/diseases-conditions/‌osteoarthritis/‌symptoms-causes/‌syc-20351925> (May 8, 2019), is relevant to show that osteoarthritis risk is increased by history of joint injuries and repeated stress on the joint.
  + New medical article, Ville M. Mattila et al., *Low Back Pain During Military Service Predicts Low Back Pain Later in Life*, 12 PLoS ONE (Mar. 2017), is relevant to show that “a history of suffering from [low back pain] seems to predict a later [low back pain] episode.”

## Ankle Disability

#### Pes Planus Causes Ankle Disability

Pes planus “may lead to profound symptoms and dysfunction that are disabling enough to incapacitate patients.” Dyan V. Flores et al., *Adult Acquired Flatfoot Deformity: Anatomy, Biomechanics, Staging, and Imaging Findings*, 39 RadioGraphics 1437, 1437 (2019), https://doi.org/10.1148/rg.2019190046 (enclosed). As pes planus progresses, it causes dysfunction of various structures of the ankle such as bone proliferation at the medial malleolus, medial soft-tissue swelling, bone hypertrophy and marrow edema at the malleolus, progressive tendon degeneration leading to elongation and tearing, accessory navicular bone, regional inflammation, spring ligament injury leading to repetitive exaggerated descent of the talar head, damage to the deep deltoid ligament causing tibiotalar joint tilting and aggravating a hindfoot valgus deformity placing tension on the tibial nerve, and many more biomechanical cascading effects. *See generally id.* at 1437–58. These abnormalities can cause symptoms of pain, swelling, malalignment, gait dysfunction, and more. *See, e.g.*, *id.* at 1444.

## Hip Disability

#### Gait and Posture Abnormalities Cause or Aggravate Hip Osteoarthritis

Medical research shows a relationship between altered gait and posture and the development or progression of hip osteoarthritis. In particular, “the hip and the spine are closely related, and as a result, changes in the postural alignment of the entire body tend to accompany hip OA progression”; “the pathologies of the hip joint and the spine are intimately related.” Hiroshige Tateuchi, *Gait- and Postural-Alignment-Related Prognostic Factors for Hip and Knee Osteoarthritis: Toward the Prevention of Osteoarthritis Progression*, 22 Phys. Therapy Research 31, 33 (2019) (enclosed). Based on a prospective cohort study, experts have concluded that “[c]hanges in the postural alignment observed in hip OA are not only related to the disturbed balance of the entire body and low back pain, but may also promote hip OA progression.” *Id.* at 33. Thus, “improving spinal alignment and mobility as well as reducing excessive cumulative hip loading could help in preventing” hip OA progression. *Id.* at 35.

* + New medical article, Hiroshige Tateuchi, *Gait- and Postural-Alignment-Related Prognostic Factors for Hip and Knee Osteoarthritis: Toward the Prevention of Osteoarthritis Progression*, 22 Phys. Therapy Research 31, 33 (2019), is relevant to show that the hip and the spine are closely related, and as a result, changes in the postural alignment of the entire body tend to accompany hip OA progression”; “the pathologies of the hip joint and the spine are intimately related.”

#### Foot pain Causes Hip Pain

* Nexus to service-connected foot disability:
  + New medical article, Alyssa B. Dufour et al., *Foot Pain in Relation to Ipsilateral and Contralateral Lower-Extremity Pain in a Population-Based Study*, 107 J. Am. Podiac. Med. Ass’n 307 (2017), is relevant to show that, “bilateral foot pain was associated with increased odds of knee and hip pain in men and women.” Researchers posit that “correlated and compensatory posture and movement theory may explain how multijoint osteoarthritis develops, as well as other pathologic abnormalities and associated pains that can result from overuse or trauma to one or more structures in the kinetic chain.”

## Knee Disability

#### Pes Planus Causes Knee and Low Back Pain

In a 2008 study of over 97,000 military recruits—about 16 percent of whom were diagnosed as having pes planus—researchers found that “[m]oderate and severe pes planus was associated with nearly double the rate of anterior knee pain and intermittent low back pain.” Yona Kosashvili et al., *The Correlation Between Pes Planus and Anterior Knee or Intermittent Low Back Pain*, 29 Foot & Ankle 910, 910 (Sept. 2008), <https://‌journals.‌sagepub.‌com/‌doi/‌full/‌10.3113/‌FAI.2008.0910> (enclosed).

* Nexus to service-connected pes planus:
  + New medical literature, Yona Kosashvili et al., *The Correlation Between Pes Planus and Anterior Knee or Intermittent Low Back Pain*, 29 Foot & Ankle 910, 910 (Sept. 2008), <https://‌journals.‌sagepub.‌com/‌doi/‌full/‌10.3113/‌FAI.2008.0910>, is relevant to show that “[m]oderate and severe pes planus was associated with nearly double the rate of anterior knee pain and intermittent low back pain.”

#### Knee Disability Causes Contralateral Knee Disability

* Nexus to service-connected contralateral knee:
  + New medical literature, Tsukasa Kamitani et al., *Contralateral Knee Pain Exacerbation*

## Foot Disabilities

#### Onset of Pes Planus

In a 2011 scientific analysis of survey data from veterans and nonveterans, researchers found that “[f]latfoot deformity and arthritis were significantly more prevalent in veterans versus nonveterans in the United States.” Naohiro Shibuya et al., *Prevalence of Podiatric Medical Problems in Veterans Versus Nonveterans*, 101 J. of Am. Podiatric Med. Ass’n 323, 323 (July/Aug. 2011), <https://www.researchgate.net/profile/Naohiro-Shibuya/‌publication/‌51547584_‌Prevalence_‌of_‌Podiatric_‌Medical_‌Problems_‌in_‌Veterans_‌versus_‌Nonveterans/‌links/‌00b4952c4594e6b4fb000000/‌Prevalence-of-Podiatric-Medical-Problems-in-Veterans-versus-Nonveterans.pdf> (enclosed).

* + New medical article, Naohiro Shibuya et al., *Prevalence of Podiatric Medical Problems in Veterans Versus Nonveterans*, 101 J. of Am. Podiatric Med. Ass’n 323, 323 (July/Aug. 2011), <https://www.researchgate.net/profile/Naohiro-Shibuya/‌publication/‌51547584_‌Prevalence_‌of_‌Podiatric_‌Medical_‌Problems_‌in_‌Veterans_‌versus_‌Nonveterans/‌links/‌00b4952c4594e6b4fb000000/‌Prevalence-of-Podiatric-Medical-Problems-in-Veterans-versus-Nonveterans.pdf>, is relevant to show that “[f]latfoot deformity and arthritis were significantly more prevalent in veterans versus nonveterans in the United States.”

#### Obesity Causes Plantar Fasciitis

Medical research has established an association between obesity and plantar fasciitis. E.R. Waclawski, *Systematic Review: Plantar Fasciitis & Prolonged Weight Bearing*, 65 Occupational Med. 97–106, 102 (2015). Based on review of four studies, researchers concluded that, in fact, there was moderate evidence that obesity causes plantar fasciitis. *Id.*

#### Onset of Plantar Fasciitis

Medical treatise evidence shows that an abnormal pattern of walking can affect the way weight is distributed and cause or aggravate plantar fasciitis. *Plantar Fasciitis*, Mayo Clinic (Dec. 11, 2019), <https://www.mayoclinic.org/diseases-conditions/plantar-fasciitis/symptoms-causes/syc-20354846> (enclosed). Further, S1 radiculopathy has been shown to be a referred cause of heel pain. Abdallah E. Allam & Ke-Vin Chang, *Plantar Heel Pain*, StatePearls (Jan. 2021), <https://www.ncbi.nlm.nih.gov/books/NBK499868/> (enclosed). And clinical guidelines for the diagnosis and treatment of plantar fasciitis show that primary risk factors for plantar fasciitis include limited ankle dorsiflexion range of motion. Thomas G. McPoil et al., *Heel Pain — Plantar Fasciitis*, 38(4) J. Orthopedic Sports Physical Therapy A1 (2008), <https://www.jospt.org/doi/pdf/10.2519/jospt.2008.0302> (enclosed).

* + New medical article, *Plantar Fasciitis*, Mayo Clinic (Dec. 11, 2019), <https://www.mayoclinic.org/diseases-conditions/plantar-fasciitis/symptoms-causes/syc-20354846>, is relevant to show that an abnormal pattern of walking can affect the way weight is distributed and cause or aggravate plantar fasciitis.
  + New medical article, Abdallah E. Allam & Ke-Vin Chang, *Plantar Heel Pain*, StatePearls (Jan. 2021), <https://www.ncbi.nlm.nih.gov/books/NBK499868/>, is relevant to show that S-1 radiculopathy can cause referred heel pain.
  + New medical article, Thomas G. McPoil et al., *Heel Pain — Plantar Fasciitis*, 38(4) J. Orthopedic Sports Physical Therapy A1 (2008), <https://www.jospt.org/doi/pdf/10.2519/jospt.2008.0302>, is relevant to show that primary risk factors for plantar fasciitis include limited ankle dorsiflexion range of motion.

## Jaw Disability

#### Anxiety Causes or Aggravates TMJ

* + New medical article, Erick Alves dos Santos et al., *Association Between Temporomandibular Disorders and Anxiety: A Systematic Review*, 13 Front. Psych. 990430 (2022), available at [https://www.ncbi.nlm.nih.gov/pmc/  
    articles/PMC9606663/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9606663/), is relevant to show that numerous studies theorize “anxiety plays an important role in TMD and can be considered as an initiating or aggravating factor” through increased jaw muscle activity and increased pain sensation.

## Spine Disability

#### Low Back Pain in Service Predicts Later Low Back Pain

A 2017 study of Finnish military servicemembers found “that unspecified [low back pain (LBP)] during military service predicts LBP in later life.” Ville M. Mattila et al., *Low Back Pain During Military Service Predicts Low Back Pain Later in Life*, 12 PLoS ONE e0173568 (2017) (enclosed). Thus, combined with the Veteran’s statements of continuous recurrent symptoms since service, the evidence is at least nearly equal to show that the current back disability is related to the in-service back pain.

#### Lumbar Scoliosis Causes Cervical Disability

Lumbar spine disabilities are shown to cause cervical spine disability over time. Mr. Archer’s medical records show that his lumbar spine condition has caused scoliosis or abnormal curvature of the spine. A 2017 observational study built on earlier limited research to show that “neck problems are more prevalent and more often coexist with back problems in individuals with idiopathic scoliosis than in controls.” Christos Topalis et al., *Neck and Back Problems in Adults with Idiopathic Scoliosis Diagnosed in Youth: An Observational Study of Prevalence, Change Over a Mean Four Year Time Period and Comparison with a Control Group*, 12 Scoliosis Spinal Disord. 20 (2017), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC5465548/> (enclosed).

#### Parachute Jumps Cause Lumbar Spine Degenerative Disease

Additional new and relevant evidence shows that back disabilities later in life are at least as likely as not related to the physical stress of frequent parachutist jumps during military service. A 2003 article describing the results of a review of the medical records of 74 military parachuting instructors found that “parachuting predisposes to spondylolysis and to degenerative changes of the lumbar spine.” Y Bar-Dayan *et al.*, *Degenerative Disease in Lumbar Spine of Military Parachuting Instructors*, 149 J.R. Army Med. Corps 260, 261 (2003), available at <https://pubmed.ncbi.nlm.nih.gov/15015796/> (enclosed). And although the researchers cited a need for further study, this evidence satisfies the very low burden Mr. Floyd must meet to show his current back disability at least as likely as not is the result of his in-service jumps.

Further, an Army Public Health Center report in 2019 found that injuries occur among U.S. paratrooper trainees at a rate of 5.5 per 1,000 jumps. *Injuries Among Military Paratroopers—Current Evidence and Data Gaps*, Tech. Info. Paper No. 12-095-0219, 4 (2019), available at <https://apps.dtic.mil/sti/citations/AD1078708> (enclosed). The report summarizes findings of several studies showing that back and neck injuries among paratroopers range from 10 to 19 percent. *Id.* at 7.

* + New medical literature, *Injuries Among Military Paratroopers—Current Evidence and Data Gaps*, Tech. Info. Paper No. 12-095-0219, 4 (2019), available at <https://apps.dtic.mil/sti/citations/AD1078708>, is relevant to show that injuries occur among U.S. paratrooper trainees at a rate of 5.5 per 1,000 jumps.

#### Pes Planus Causes Knee and Low Back Pain

In a 2008 study of over 97,000 military recruits—about 16 percent of whom were diagnosed as having pes planus—researchers found that “[m]oderate and severe pes planus was associated with nearly double the rate of anterior knee pain and intermittent low back pain.” Yona Kosashvili et al., *The Correlation Between Pes Planus and Anterior Knee or Intermittent Low Back Pain*, 29 Foot & Ankle 910, 910 (Sept. 2008), <https://‌journals.sagepub.com/‌doi/‌full/‌10.3113/FAI.2008.0910> (enclosed).

* + New medical article, Yona Kosashvili et al., *The Correlation Between Pes Planus and Anterior Knee or Intermittent Low Back Pain*, 29 Foot & Ankle 910, 910 (Sept. 2008), <https://‌journals.sagepub.com/‌doi/‌full/‌10.3113/FAI.2008.0910>, is relevant to show that a 2008 study of over 97,000 military recruits—about 16 percent of whom were diagnosed as having pes planus—researchers found that “[m]oderate and severe pes planus was associated with nearly double the rate of anterior knee pain and intermittent low back pain.” Thus an altered gait is not even necessarily required for causation or aggravation by pes planus.

#### Stress and Inactivity Cause Neck Pain

* Nexus to service-connected disabilities through stress and physical inactivity:
  + New medical literature, Pekka Mantyselka, *et al.*, *Prevalence of Neck Pain in Subjects with Metabolic Syndrome – A Cross-Sectional Population-Based Study*, 11 BMC Musc. Disords. 171 (2010), available at <https://pmc.ncbi.nlm.nih.gov/articles/PMC2918543/>, is relevant to show that based on preliminary study, researchers hypothesize that neck pain and metabolic syndrome share a common pathway: stress and physical inactivity. “A large epidemiological follow-up study indicated that physical inactivity is related to chronic musculoskeletal complaints.”

# Organs of the Special Sense

# Impairment of Auditory Acuity

## Hearing Loss

#### Noise-Induced Hearing Loss After Temporary Threshold Shifts

There are generally considered to be two types of injury due to noise exposure: temporary threshold shift (TTS), and permanent threshold shift. Trung N Le et al, *Current Insights in Noise-Induced Hearing Loss: A Literature Review of the Underlying Mechanism, Pathophysiology, Asymmetry, and Management Options*, 46 J. of Otolaryngology – Head & Neck Surgery 41 (2017) (enclosed). But “recent studies . . . have found TTS’s at young ages accelerated age-related hearing loss.” *Id.* Thus, even when puretone thresholds completely return to normal shortly after hazardous noise exposure, “there can be considerable damage to the ribbon synapses, a rapid degeneration termed synaptopathy . . . . This is also referred to as Noise-Induced Hidden Hearing Loss, as it is not accompanied by a pure-tone threshold shift.” *Id.* Thus, the National Institutes of Health have concluded that in cases of temporary hearing loss, “although the loss of hearing seems to disappear, there may be residual long-term damage to your hearing.” *NIDCD Fact Sheet: Noise-Induced Hearing Loss*, Nat’l Inst. on Deafness & Other Comm. Disords., NIH Pub. No. 99-4233 (reprinted in June 2019) (enclosed).

Therefore, the most accurate and up-to-date research shows that the absence of a pure-tone threshold shift at the time the Veteran exited service, or other evidence that in-service threshold shifts were temporary, is not evidence weighing against a causative nexus. In other words, the factual basis for the opining clinician’s conclusion was false and the opinion is inadequate.

* + New medical article Trung N Le et al, *Current Insights in Noise-Induced Hearing Loss: A Literature Review of the Underlying Mechanism, Pathophysiology, Asymmetry, and Management Options*, 46 J. of Otolaryngology – Head & Neck Surgery 41 (2017), is relevant to show that even when puretone thresholds completely return to normal shortly after hazardous noise exposure, “there can be considerable damage to the ribbon synapses, a rapid degeneration termed synaptopathy . . . . This is also referred to as Noise-Induced Hidden Hearing Loss, as it is not accompanied by a pure-tone threshold shift.”
  + New medical article *NIDCD Fact Sheet: Noise-Induced Hearing Loss*, Nat’l Inst. on Deafness & Other Comm. Disords., NIH Pub. No. 99-4233 (reprinted in June 2019), is relevant to show that in cases of temporary hearing loss, “although the loss of hearing seems to disappear, there may be residual long-term damage to your hearing.”

#### Military Noise Exposure Causes Hearing Loss

According to The Journal of Neuroscience “Results suggest that nose-induced damage to the ear has progressive consequences that are considerably more widespread than are revealed by conventional threshold testing. This primary neurodegeneration should add to difficulties hearing in noisy environments, and could contribute totinnitus, hyperacusis and other perceptual anomalies commonly associated with inner ear damage”.

“Adding Insult to Injury: Cochlear Nerve Degeneration after “Temporary” Noise-Induce Hearing Loss”. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2812055/>

Much of the noise experienced by military personnel exceeds that of maximum protection achievable with double hearing protection. Military personnel have little option but to remain in noisy environments in order to complete their missions.

“Impact of noise on hearing in the military”. [Impact of noise on hearing in the military | Military Medical Research | Full Text (biomedcentral.com)](https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-015-0034-5#:~:text=Noise-induced%20hearing%20loss%20is%20a%20significant%20impairment%20in,tinnitus%20remain%20the%20second%20most%20prevalent%20service-connected%20disabilities.)

## Peripheral Vestibular Disorders

* Nexus to service-connected TBI:
  + New medical article, Gerard J. Gianoli, *Post-Concussive Dizziness: A Review and Clinical Approach to the Patient*, 12 Frontiers in Neuro. 718318 (2022), available at <https://pmc.ncbi.nlm.nih.gov/articles/PMC8764304/>, is relevant to show that “[a]mong patients who suffer a concussion (mild traumatic brain injury or mTBI), dizziness is second only to headache in symptom frequency.”

# Infections Diseases, Immune Disorders, and Nutritional Deficiencies

## Immune Disability

#### Jet Fuel Causes Immunotoxicity

Exposure to potential environmental toxicants such as jet fuel may have significant effects on host systems beyond those readily visible (e.g., physiology, cardiology, respiratory, etc.) e.g. the immune system. Significant changes in immune function, even if short-lived, may have serious consequences for the exposed host.

“Jet fuel-induced immunotoxicity”. [Jet fuel-induced immunotoxicity - PubMed (nih.gov)](https://pubmed.ncbi.nlm.nih.gov/11693943/#:~:text=Jet%20fuel-induced%20immunotoxicity%20Chronic%20exposure%20to%20jet%20fuel,fuel%20may%20have%20significant%20effects%20on%20hos%20%E2%80%A6)

#### PFAS Causes Decreased Antibody Response

*Guidance on PFAS Exposure, Testing, and Clinical Follow-Up 2022*, Nat’l Acads. Scis. Comm. on Guidance on PFAS Testing & Health Outcomes (2022), available at <https://nap.naptionalacademies.org/26156> (enclosed).

# Respiratory

## Obstructive Sleep Apnea (OSA)

#### Antidepressants Cause Obstructive Sleep Apnea (OSA)

The Veteran is entitled to service connection for OSA on a secondary basis because medical evidence shows it is at least as likely as not that his OSA disability was either caused by or aggravated by the *[Veteran’s service-connected depression disability or]* medications taken to treat service-connected depression.

*[insert depression research (below) here if Veteran is service-connected for depression and edit as needed]*

A 2017 review of recent medical studies on the effects of antidepressant medication on sleep found that certain antidepressants—notably serotonin and norepinephrine reuptake inhibitors (SNRI), norepinephrine reuptake inhibitors (NRI), monoamine oxidase inhibitors (MAOI), selective serotonin reuptake inhibitors (SSRI), and activating tricyclic antidepressants (TCA)—may deteriorate sleep quality. Adam Wichniak et al., *Effects of Antidepressants on Sleep*, 19:63 Sleep Disorders (2017), 2, available at <https://link.springer.com/‌content/‌pdf/‌10.1007/‌s11920-017-0816-4.pdf> (enclosed). Another research review conducted in 2009 noted that “tricyclic and selective serotonin reuptake inhibitor antidepressants may also lower sleep efficiency in patients with OSA.” Melanie Harris et al., *Obstructive Sleep Apnea and Depression*, 13 Sleep Medicine Reviews 437, 441 (2009) (enclosed).

Further, the Veteran is taking the medication Xanax. Medical research shows that benzodiazepines like Xanax may “cause health problems, such as complete obstructive sleep apnea” in certain patients. C. Guilleminault, *Benzodiazepines, Breathing, and Sleep*, 88 Am. J. Med. 25S (1990), available at <https://pubmed.ncbi.nlm.nih.gov/1968716/> (abstract enclosed). In addition, in patients with sleep apnea, benzodiazepines are shown to worsen their condition, potentially causing acute respiratory failure. Sheng-Huie Wang et al., *Benzodiazepines Associated with Acute Respiratory Failure in Patients with Obstructive Sleep Apnea*, 9 Front Pharmacol. 1513 (2019), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC6330300/> (enclosed).

This scientific research thus indicates that there may be an association between the Veteran’s service-connected depression disability (and the medications used to treat that disability) and his current OSA. The record shows that the Veteran has been prescribed sertraline, an SSRI (*Sertraline*, NHS (last updated Dec. 12, 2018), https://www.nhs.uk/‌medicines/‌sertraline/), during the period on appeal.

Because the medical research shows that SSRIs can deteriorate sleep quality, resolving reasonable doubt in the Veteran’s favor it is at least as likely as not that the Veteran’s service-connected depression disability caused or aggravated his current OSA disability. In the alternative, if the evidence is not sufficient to grant service connection, a medical opinion is necessary to determine whether it is at least as likely as not that the Veteran’s SSRI use for service-connected depression caused or aggravated the Veteran’s current OSA. *See McLendon v. Nicholson*, 20 Vet. App. 79, 81 (2006).

* Nexus to service-connected mental health through medication:
  + The Veteran is prescribed medication for mental health. New article Adam Wichniak et al., *Effects of Antidepressants on Sleep*, 19:63 Sleep Disorders (2017), available at <https://link.springer.com/‌content/‌pdf/‌10.1007/‌s11920-017-0816-4.pdf>, is relevant to show that SSRIs, NRIs, MAOIs, SNRIs, and TCAs deteriorate sleep quality.

#### Asthma Aggravates or Causes OSA

* Nexus to service-connected asthma:
  + New medical article, Bharati Prasad et al., *Asthma and Obstructive Sleep Apnea Overlap*, 201 Am. J. Resp. Crit. Care Med. 1345 (2020), is relevant to show that there are consistently higher burdens of apnea among asthma patients and plausible interactive mechanisms including “airway and systemic inflammation, neuroimmune interactions, and effects of asthma-controlling medications (corticosteroids) as factors that predispose patients with asthma to OSA.”

#### At-Home Sleep Test Without Mask Inadequate

* + New medical article, *What to Know About an At-Home Sleep Test*, Johns Hopkins Medicine, <https://www.hopkinsmedicine.org/health/wellness-and-prevention/what-to-know-about-an-at-home-sleep-test> (last visited Apr. 28, 2025), is relevant to show that a sleep test must include a mask to measure pauses in breathing. Without a mask, there’s no way for the pulse oximeter alone to measure breathing and the C&P exam was entirely inadequate.
  + New medical article, *What to Know About an At-Home Sleep Test*, Johns Hopkins Medicine, <https://www.hopkinsmedicine.org/health/wellness-and-prevention/what-to-know-about-an-at-home-sleep-test> (last visited Apr. 28, 2025), is also relevant to show that an at-home sleep test is not a full picture of sleep quality or actually of sleep at all. The test has no way to know when the subject is asleep.

#### COPD Causes Sleep Apnea

Medical research shows there are many ways in which COPD and OSA are interrelated. In fact, coexistence of these disabilities is so common they are given the combined name of overlap syndrome. *See* Robert L. Owens & Atul Malhotra, *Sleep-Disordered Breathing and COPD: The Overlap Syndrome*, 55 Respir Care 1333 (2010). Researchers have posited that COPD may “cause or exacerbate” OSA by causing skeletal-muscle myopathy, or that inhaled corticosteroids to treat COPD could cause pharyngeal muscle myopathy. *Id.* Further, in patients with “right-heart failure, redistribution of edema fluid during supine sleep might also contribute to OSA.” *Id.* A patient with COPD “has a greater than 10% chance of also having COPD. *Id.*

#### Depression Causes Obstructive Sleep Apnea (OSA)

In the alternative, the Veteran is entitled to service connection for OSA on a secondary basis because medical evidence shows it is at least as likely as not that his OSA disability was either caused by or aggravated by the Veteran’s depression.

A 2009 review of medical research noted that “[p]atients who have depression as well as OSA appear worse off than those with OSA only.” Melanie Harris et al., *Obstructive Sleep Apnea and Depression*, 13 Sleep Medicine Reviews 437, 437 (2009) (enclosed). Further, prospective longitudinal studies showed that, controlling for body mass index, alcohol consumption, and cardiovascular disease showed an association between OSA severity and depression. *Id.* at 440. Further, “[c]omorbid depression has been found to impact adversely on self-management, treatment adherence and functioning and to increase symptom perception” in other disabilities, and may also be true of OSA. *Id.* at 442. “OSA patients with high levels of depression are those with most daytime sleepiness,[] fatigue,[] and lowest quality of life scores.” *Id.* (footnotes omitted).

*[insert antidepressant research (above) here if Veteran is service-connected for depression and edit as needed]*

Because the medical research shows that patients with depression have worse OSA symptoms, resolving reasonable doubt in the Veteran’s favor it is at least as likely as not that the Veteran’s service-connected depression disability caused or aggravated his current OSA disability. In the alternative, if the evidence is not sufficient to grant service connection, a medical opinion is necessary to determine whether it is at least as likely as not that the Veteran’s service-connected depression caused or aggravated the current OSA disability. *See McLendon v. Nicholson*, 20 Vet. App. 79, 81 (2006).

* Nexus to service-connected depression:
  + New medical literature, Melanie Harris et al., *Obstructive Sleep Apnea and Depression*, 13 Sleep Medicine Reviews 437 (2009), is relevant to show that “[p]atients who have depression as well as OSA appear worse off than those with OSA only.” Further, “[c]omorbid depression has been found to impact adversely on self-management, treatment adherence and functioning and to increase symptom perception” in other disabilities, and may also be true of OSA.

#### In-Service Snoring is Early Onset

Medical treatise evidence enclosed shows that although snoring alone is not sufficient to definitively imply the presence of obstructive sleep apnea, it is the most common symptom of apnea. Abdulsalam Saif Ibrahim et al., *Predictors of Obstructive Sleep Apnea in Snorers*, 27 Ann. Saudi Med. 421 (2007), available at <https://www.ncbi.nlm.nih.gov/pmc/‌articles/‌PMC6074179/> (enclosed). When combined with other screening factors, a history of snoring in fact becomes a powerful predictive tool for sleep apnea; witnessed apneas in particular—such as those competently observed during the Veteran’s service—are a strong predictor of the presence of obstructive sleep apnea. *Id.* Further, “[r]esearchers estimate that 82% of men and 93% of women with moderate-to-severe OSAS have not been clinically detected or diagnosed.” *Id.*at 424–24. Thus, there is a significant medical plausibility that witnessed snoring and apneas in service indicate that the Veteran’s apnea disability had already manifested by that time, but went undiagnosed.

* + New medical article, Abdulsalam Saif Ibrahim et al., *Predictors of Obstructive Sleep Apnea in Snorers*, 27 Ann. Saudi Med. 421 (2007), available at <https://www.ncbi.nlm.nih.gov/pmc/‌articles/‌PMC6074179/>, is relevant to show that although snoring alone is not sufficient to definitively imply the presence of obstructive sleep apnea, it is the most common symptom of apnea.

#### Lung Disease Causes Obstructive Sleep Apnea (OSA)

The Veteran is service-connected for restrictive lung disease. Medical research shows that interstitial lung disease is a risk factor for sleep disordered breathing. Lauren K Troy & Tamera J Corte, *Sleep Disordered Breathing in Interstitial Lung Disease: A Review*, 2 World J. Clin. Cases 828 (2014), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC4266829/‌pdf/WJCC-2-828.pdf> (enclosed). “[I]t is believed that reduced caudal traction on the upper airway can enhance collapsibility.” *Id.* at 828.

#### Neck Disability Causes Sleep Apnea

Medical research has suggested a connection between various cervical spine pathologies and the development of obstructive sleep apnea. For example, patients with rheumatoid arthritis affecting the occiput-C1 and C1-C2 synovial articulations may have “subluxation of the vertebrae and vertical translation, leading to reduced neck width and a decreased angle of the cranio-vertebral junction,” causing physical shifts that “may help account for the larger prevalence of sleep apnea in RA patients.” Adam Khan, *Sleep Apnea and Cervical Spine Pathology*, 23 Eur. Spine J. 641 (2014), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC3940806/pdf/586_2013_Article_3046.pdf> (enclosed).

* Nexus to service-connected neck disability:
  + New article Adam Khan, *Sleep Apnea and Cervical Spine Pathology*, 23 Eur. Spine J. 641 (2014), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC3940806/pdf/586_2013_Article_3046.pdf>, is relevant to show that physical shifts due to cervical spine disabilities “may help account for the larger prevalence of sleep apnea in [these] patients.”

#### Obesity Causes Obstructive Sleep Apnea (OSA)

*[insert text connecting service-connected disability to obesity]*

“There is a linear correlation between obesity and OSA.” Shazia Jehan et al., *Obstructive Sleep Apnea and Obesity: Implications for Public Health*, Sleep Med. Disord. (2017), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/‌PMC5836788/pdf/nihms932293.pdf> (enclosed). And the more obese a person is, the more severe their sleep apnea becomes. *Id.* This is because “fat deposits in the upper respiratory tract narrow the airway; there is a decrease in muscle activity in this region, leading to hypoxic and apneic episodes, ultimately resulting in sleep apnea.” *Id.*

The medical evidence thus establishes with sufficient certainty a causal relationship between PTSD and obesity, and obesity and sleep apnea. Given this convincing medical consensus and the evidence of record in this case, resolving all doubt in the Veteran’s favor service connection must be granted for sleep apnea as secondary to service-connected PTSD.

* + New article Shazia Jehan et al., *Obstructive Sleep Apnea and Obesity: Implications for Public Health*, Sleep Med. Disord. (2017), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5836788/pdf/nihms932293.pdf>, is relevant to show that “fat deposits in the upper respiratory tract narrow the airway; there is a decrease in muscle activity in this region, leading to hypoxic and apneic episodes, ultimately resulting in sleep apnea.”

#### Particulate Matter Causes Obstructive Sleep Apnea (OSA)

The evidence enclosed here supports direct service connection for sleep apnea due to exposure to particulate matter. Under 38 C.F.R. § 3.320, a veteran with any period of active service in Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, the Red Sea, or the airspace above these locations during the Persian Gulf War (August 2, 1990, to present), or with active service in Afghanistan, Syria, Djibouti, or Uzbekistan on or after September 19, 2001, is legally presumed to have been exposed to fine, particulate matter during service unless evidence shows otherwise.

The Veteran has qualifying service set forth above and is therefore presumed to have been exposed to particulate matter.

Medical research shows that long-term exposure to particulate matter air pollution is associated “with 39% greater adjusted odds of sleep apnea,” and therefore researchers have concluded that “[i]n addition to individual risk factors, environmental factors also contribute to the variation of sleep disorders across groups.” Martha E. Billings et al., *The Association of Ambient Air Pollution with Sleep Apnea: The Multi-Ethnic Study of Atherosclerosis*, 16 AnnalsATS 363, 363 (Mar. 2019), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC6394120/pdf/AnnalsATS.201804-248OC.pdf> (enclosed). The researchers’ analysis of longitudinal study of human subjects and experimentation in mammals led them to conclude that potential mechanisms for this association included “upper airway edema, inflammation, and irritation . . . , which may contribute to upper airway obstruction during sleep.” *Id.* at 367.

* Nexus to particulate-matter exposure:
  + New medical article, Martha E. Billings et al., *The Association of Ambient Air Pollution with Sleep Apnea: The Multi-Ethnic Study of Atherosclerosis*, 16 AnnalsATS 363, 363 (Mar. 2019), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6394120/pdf/AnnalsATS.201804-248OC.pdf>, is relevant to show that long-term exposure to particulate matter air pollution is associated “with 39% greater adjusted odds of sleep apnea,” and therefore researchers have concluded that “[i]n addition to individual risk factors, environmental factors also contribute to the variation of sleep disorders across groups.”

#### PTSD Causes Obstructive Sleep Apnea (OSA)

In a 2015 study of Iraq and Afghanistan veterans, researchers found that “PTSD symptom severity increased the risk of screening positive for [obstructive sleep apnea (OSA)]. . . . at much higher rates than those seen in community studies” and that those veterans may need different types of screening to diagnosis OSA as they tend not to show the classic predictors of OSA. Peter J. Colvonen et al., *Obstructive Sleep Apnea and Posttraumatic Stress Disorder Among OEF/OIF/OND Veterans*, 11 J. of Clinical Sleep Med. 513, 513 (2015), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC4410924/‌pdf/jcsm.11.5.513.pdf> (enclosed).

Based on this medical treatise evidence and the evidence of continuous symptoms since the onset of the Veteran’s service-connected PTSD, it is at least as likely as not that the Veteran’s current sleep apnea is caused or aggravated by his PTSD. The medical treatise evidence also explains why the Veteran’s symptoms of sleep apnea may have gone undiagnosed for some time following service—as screening for sleep apnea in veterans with PTSD is more difficult than in the general population. *See id.*

* Nexus to service-connected PTSD:
  + New medical article, Peter J. Colvonen et al., *Obstructive Sleep Apnea and Posttraumatic Stress Disorder Among OEF/OIF/OND Veterans*, 11 J. of Clinical Sleep Med. 513, 513 (2015), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4410924/pdf/jcsm.11.5.513.pdf>, is relevant to show that “PTSD symptom severity increased the risk of screening positive for [obstructive sleep apnea (OSA)]. . . . at much higher rates than those seen in community studies” and that those veterans may need different types of screening to diagnosis OSA as they tend not to show the classic predictors of OSA.
  + New medical article, Madhulike A Gupta & Fiona C. Simpson, *Obstructive Sleep Apnea and Psychiatric Disorders: A Systematic Review*, 11 J. Clinical Sleep Med. 165 (2015), is relevant to show that PTSD and MDD increase the prevalence of sleep apnea. The researchers explain a number of mechanisms are plausible, including PTSD and MDD contributing to obesity, smoking, and cardiovascular problems which then cause apnea. However the researchers also explain that “Central nervous system (CNS) alterations in psychiatric disorders may also lead to an increased risk of OSA, as sympathetic hyperactivity and hyperarousal states and resultant sleep fragmentation may lead to upper airway instability.”

#### TBI Causes Sleep Apnea

The enclosed new and relevant medical treatise evidence shows that “[s]leep disturbances after TBI are estimated to occur in 30–70% of head injured patients.” Mari Viola-Saltzman and Nathaniel F. Watson, *Traumatic Brain Injury and Sleep Disorders*, 30 Neurol. Clin. 1299 (2012), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC3482689/‌pdf/‌nihms400055.pdf> (enclosed). This research states that TBI-related injuries to the “[h]igh cervical cord . . . have also been known to cause sleepiness and obstructive sleep apnea.” *Id.*

Thus, it is at least as likely as not that the Veteran’s service-connected TBI caused or aggravated his current sleep apnea disability.

* Nexus to service-connected TBI:
  + New medical literature, Mari Viola-Saltzman and Nathaniel F. Watson, *Traumatic Brain Injury and Sleep Disorders*, 30 Neurol. Clin. 1299 (2012), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC3482689/‌pdf/‌nihms400055.pdf>, is relevant to show that “[s]leep disturbances after TBI are estimated to occur in 30–70% of head injured patients.” This research states that TBI-related injuries to the “[h]igh cervical cord . . . have also been known to cause sleepiness and obstructive sleep apnea.”

#### Volatile Organic Compounds Cause or Aggravate Sleep Apnea

* Nexus to Camp Lejeune exposure:
  + New medical literature, Jianyun Sun *et al.*, *Association Between Volatile Organic Compounds and the Prevalence of Sleep Problems in U.S. Adults*, 12 Toxics 222 (2024), is relevant to show that “VOCs may have a direct effect on the central nervous system, resulting in altered and dysregulated neurochemical expression. Specifically, the penetration of VOCs into the brain alters serotonin levels, disrupts the protective epithelial barrier, and destroys nerve cells. These alterations may interfere with brain function and cause sleep problems.”

#### Rhinitis & Sinusitis Aggravate Sleep Apnea

* Nexus to service-connected rhinitis/sinusitis:
  + New medical article, G. Magliulo et al., *Nasal Pathologies in Patients with Obstructive Sleep Apnoea*, 39 Acta Otorhino. Italica 250 (2019), is relevant to show that, “Various authors have supported the theory that nasal obstruction is a contributing factor in the pathogenesis of OSA despite numerous controversies  6-10. Nasal obstruction leads to mouth breathing, which is thought to destabilise the upper airway and aggravate OSA.”

#### Tinnitus Causes or Aggravates Sleep Apnea

Medical research shows that tinnitus has a correlation with sleep disorders. “Difficulty initiating sleep, difficulty maintaining sleep and a poor perceived quality of sleep are frequently encountered in patients with tinnitus.” H. Koning, *Sleep Disturbances Associated with Tinnitus: Reduce the Maximal Intensity of Tinnitus*, Int. Tinnitus J. 23(1): 64, 64 (2019), DOI: 10.5935/946-5448.20190012, available at <https://www.tinnitusjournal.com/articles/sleep-disturbances-associated-with-tinnitus-reduce-the-maximal-intensity-of-tinnitus.pdf> (enclosed).This cohort study found that half of the tinnitus patients experienced sleep quality issues. *Id*. at 67. The worse the tinnitus, the worse the sleep quality. *Id.*

A 2017 study of 173 patients with chronic tinnitus found that tinnitus resulted in worse symptoms of sleep disordered breathing. J-T Lai et al., *Higher Prevalence and Increased Severity of Sleep-Disordered Breathing in Male Patients with Chronic Tinnitus: Our Experience with 173 Cases*, 43 Clin. Otolaryngology 772 (2018), available at <https://‌onlinelibrary.‌wiley.com/‌doi/‌10.1111/‌coa.13024> (enclosed). More than 65 percent of the tinnitus patients had AHI over 15. *Id.* at 723. The authors also found that “[sleep disordered breathing] is much more common and severe in men with tinnitus.” *Id.* at 724 Furthermore, the believe that “tinnitus and [sleep disordered breathing] may be two sides of the same coin; that is, they are either co-morbidities or aetiologically related.” *Id.*

This new and relevant evidence shows that Veteran’s tinnitus likely caused or aggravated his sleep apnea. Accordingly, he is entitled to service connection for his sleep apnea secondary to his service-connected tinnitus.

* Nexus to service-connected tinnitus:
  + New medical article, H. Koning, *Sleep Disturbances Associated with Tinnitus: Reduce the Maximal Intensity of Tinnitus*, Int. Tinnitus J. 23(1): 64, 64 (2019), DOI: 10.5935/946-5448.20190012, available at <https://www.tinnitusjournal.com/articles/sleep-disturbances-associated-with-tinnitus-reduce-the-maximal-intensity-of-tinnitus.pdf>, is relevant to show that Difficulty initiating sleep, difficulty maintaining sleep and a poor perceived quality of sleep are frequently encountered in patients with tinnitus.”
  + New medical article, J-T Lai et al., *Higher Prevalence and Increased Severity of Sleep-Disordered Breathing in Male Patients with Chronic Tinnitus: Our Experience with 173 Cases*, 43 Clin. Otolaryngology 772 (2018), available at <https://‌onlinelibrary.‌wiley.com/‌doi/‌10.1111/‌coa.13024>, is relevant to show that tinnitus results in worse symptoms of sleep disordered breathing.

## COPD

#### Agent Orange Causes COPD

* + New medical literature enclosed, Yong C Lee et al., *2,3,7,8-Tetrachlorodibenzo-p-dioxin-Induced* MUC5AC *Expression*, 45 Am. J. Respir. Cell Mol. Biol. 270 (2011), available at [https://www.ncbi.nlm.nih.gov/pmc/  
    articles/PMC3175556/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3175556/), is relevant to show that exposure to dioxin—an herbicide agent in Agent Orange—is significantly linked with developing COPD and worse COPD outcomes.

#### Obesity Causes or Aggravates COPD

* + New medical literature, Corrine Hanson et. al., *Influence of Diet and Obesity on COPD Development and Outcomes*, 9 Int. J. Chron. Obstruct. Pulm. Dis. 723 (2014), concludes that obesity appears to play a role in the pathophysiology of COPD. Researchers concluded that obesity has an effect on lung function after review of many studies on the subject and that obesity may both create pathophysiology associated with COPD and that it worsens outcomes in COPD. Although researches concede that the data for a causal relation is not yet conclusive, “the data exist to suggest a link between these factors.” This is sufficient to meet the low VA threshold for service connection of evidence at least nearly in equipoise.

#### Particulate Matter Causes COPD

## Pulmonary Fibrosis

#### Agent Orange Causes PF

A 2022 study using data from the Veterans Health Administration comparing the prevalence of idiopathic pulmonary fibrosis among 3.6 million dioxin-exposed Veterans with non-exposed Army Veterans found a 1.14 odds ratio of increased prevalence among the exposed group. Bhavika Kaul et al,. *Agent Orange Exposure and Risk of Idiopathic Pulmonary Fibrosis Among U.S. Veterans*, 206 Am. J. Resp. Critical Care Med. 750, 750 (2022), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9799114/>. “The relationship persisted after adjusting for known IPF risk factors.” Exposure was associated with a 14% increased risk of developing idiopathic pulmonary fibrosis. *Id.* at 754. The study went so far as to identify several possible causal mechanisms supported by animal research, including immunotoxicity as a result of exposure to dioxin. *Id.* at 755.

## Rhinitis and Sinusitis

#### Differential Diagnosis of Rhinitis and Sinusitis

* + New medical literature, Mark S. Dykewicz, *Rhinitis and Sinusitis*, 111 J. Allergy Clin. Immunol. S520 (2003), is relevant to delineate the overlapping and separate symptoms of the varying types of rhinitis and chronic sinusitis (also known as rhinosinusitis) conditions. Allergic rhinitis—characterized by pathophysiological nasal inflammation—causes rhinorrhea, nasal congestion, sneezing, and nasal itching. Rhinitis is typically diagnosed by history of symptoms, precipitating factors, environmental history, and presence of other common allergy symptoms. Chronic sinusitis, on the other hand, is inflammation of one or more paranasal sinuses, typically causing nasal mucosal edema, sinus tenderness, and purulent nasal secretions. Diagnostic testing for sinusitis includes imaging, which would typically reveal opacification/air fluid levels in any paranasal sinuses, mucosal thickening in the maxillary sinuses, or loss of air space volume within the maxillary sinuses. And CT scans can identify forms of sinusitis—for example sinus ostia—not shown on standard radiographs. Nasal cytology can also help distinguish between rhinitis and sinusitis.

# Cardiovascular

#### Obesity Causes Cardiovascular Disability

#### Psychiatric Disorder Causes Cardiovascular Disability

The Veteran is entitled to service connection for cardiac disability secondary to a service-connected psychiatric disorder. The new and relevant medical treatise evidence enclosed offers ample support for secondary causation or aggravation.

“A large and growing body of research shows that mental health is associated with risk factors for heart disease before a diagnosis of a mental health disorder and during treatment. These effects can arise both directly, through biological pathways, and indirectly, through risky health behaviors.” *Heart Disease and Mental Health Disorders*, CDC, <https://www.cdc.gov/‌heartdisease/‌mentalhealth.htm> (May 6, 2020) (enclosed). In fact, research by the National Center for PTSD within the VA acknowledges that “psychological trauma and subsequent, repeated reminders of traumatic events trigger a cascade of neuronal, hormonal, and immunologic effects that damage the body over time.” Melanie Arenson and Beth Cohen, *Posttraumatic Stress Disorder and Cardiovascular Disease*, 28 PTSD Research Quarterly 1050 (2017) (enclosed). This VA-endorsed medical research identifies many potential mechanisms underlying a causative relationship between PTSD and cardiovascular disability, “including inflammation . . . , altered autonomic nervous system and neurochemical function . . . , and health behaviors.” And further research shows that PTSD “symptoms may significantly increase cardiac arrest survivors’ risk of major cardiovascular events and death up to a year after the initial medical crisis.” *PTSD Linked to Increased Complications and Death a Year After Cardiac Arrest: Am. Heart Ass’n Mtg. News Br. – Presentation 13, Session: 09*, Am. Heart Ass’n, <https://newsroom.heart.org/‌news/‌ptsd-linked-to-increased-complications-and-death-a-year-after-cardiac-arrest> (Nov. 5, 2018) (enclosed).

Thus it is at least as likely as not that the Veteran’s service-connected PTSD caused or aggravated his cardiac disability.

* Nexus to service-connected mental health:
  + New medical literature, *Heart Disease and Mental Health Disorders*, CDC, <https://www.cdc.gov/‌heartdisease/‌mentalhealth.htm> (May 6, 2020), is relecant to show that “A large and growing body of research shows that mental health is associated with risk factors for heart disease before a diagnosis of a mental health disorder and during treatment. These effects can arise both directly, through biological pathways, and indirectly, through risky health behaviors.”
  + New medical literature, Melanie Arenson and Beth Cohen, *Posttraumatic Stress Disorder and Cardiovascular Disease*, 28 PTSD Research Quarterly 1050 (2017), is relevant to show that “psychological trauma and subsequent, repeated reminders of traumatic events trigger a cascade of neuronal, hormonal, and immunologic effects that damage the body over time.”
  + New medical literature, *PTSD Linked to Increased Complications and Death a Year After Cardiac Arrest: Am. Heart Ass’n Mtg. News Br. – Presentation 13, Session: 09*, Am. Heart Ass’n, <https://newsroom.heart.org/‌news/‌ptsd-linked-to-increased-complications-and-death-a-year-after-cardiac-arrest> (Nov. 5, 2018), is relevant to identify potential mechanisms underlying a causative relationship between PTSD and cardiovascular disability, “including inflammation . . . , altered autonomic nervous system and neurochemical function . . . , and health behaviors.” And further research shows that PTSD “symptoms may significantly increase cardiac arrest survivors’ risk of major cardiovascular events and death up to a year after the initial medical crisis.”

## Atherosclerosis

#### Hepatitis B Causes Atherosclerosis

* + New medical article, Ivan Ranković et al., *Interplay Between Chronic Hepatitis B and Atherosclerosis*, 28 World J. Gastroenterol. 497 (2022), is relevant to show that hepatitis B-“induced infglammation is one of the root causes of atherosclerosis.”

## Deep-Vein Thrombosis

#### IBS Causes Deep-Vein Thrombosis

A connection between irritable bowel disease (IBD) and venous thromboembolism (VTE) has been established since it was first described in 1936. Martina Giannotta et al., *Thrombosis in Inflammatory Bowel Diseases: What’s the Link?*, 13 Thrombosis J. 1 (2015). “The risk of VTE in lower extremities and pulmonary embolism in IBD patients is reported to be 3-fold increased compared to the general population . . . even after correction for known pro-thrombotic factors.” *Id.*

## Hypertension/High Blood Pressure

#### Agent Orange Causes Hypertension

In 2018, the National Academies of Sciences, Engineering and Medicine (NAS) upgraded hypertension from its previous classification in the category of limited or suggestive evidence to sufficient evidence of an association with exposure to Agent Orange and other herbicide agents used during the Vietnam War. *Veterans & Agent Orange: Update 11*, Nat’l Acad. of Scis. 10 (2018). NAS states that this category indicates that there is enough epidemiologic evidence to conclude that there is a positive association between hypertension and herbicide agent exposure. Based on NAS findings of sufficient—or even limited or suggestive—evidence of an association to Agent Orange, VA already provides for presumptive service connection for AL amyloidosis, Hodgkin and non-Hodgkin lymphoma, Parkinson’s disease and Parkinsonism, early-onset peripheral neuropathy, porphyria cutanea tarda, prostate cancer, bladder cancer, ischemic heart disease, hypothyroidism, chlorachne, and others. *Compare id.* at 7, *with* 38 C.F.R. § 3.309. By the same logic, the medical evidence strongly supports the plausibility of service connection for hypertension for veterans exposed to herbicide agents.

#### Asbestos Causes Cardiovascular Disability

In a 2015 meta-analysis of 16 studies across the world, researchers determined “that asbestos exposure significantly increased the risk of cardiovascular related diseases in exposed workers.” Yi Rong et al., *Occupational Exposure to Asbestos and Cardiovascular Related Diseases: A Meta-Analysis*, 2 Preventative Med. Reps. 920, 920–21 (Oct. 21, 2015), <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC4721368/‌pdf/main.pdf>.

* Nexus to asbestos exposure:
  + New medical literature, Yi Rong et al., *Occupational Exposure to Asbestos and Cardiovascular Related Diseases: A Meta-Analysis*, 2 Preventative Med. Reps. 920 (Oct. 21, 2015), available at <https://pmc.ncbi.nlm.nih.gov/articles/PMC4721368/>, is relevant to show “that asbestos exposure significantly increased the risk of cardiovascular related diseases in exposed workers.”

#### Buproprion Causes High Blood Pressure

Buproprion—with brand names Wellbutrin SR, Wellbutrin XL, Aplenzin, and Forfivo XL—is known to “cause severe high blood pressure.” *Femi Aremu*, Healthline (July 27, 2021) https://www.healthline.‌com/‌‌health/buproprion-oral-tablet#important-warnings (enclosed).

#### Depression and Anxiety, or Medications to Treat, Cause Hypertension

The Veteran is entitled to service connection for the current hypertension disability because medical research shows that hypertension is caused by or aggravated by depression or medications to treat depression.

A study published in 2013 has shown that “both depression and anxiety were positively associated with hypertension status” five years later among a group of 455 participants after controlling for variables including “age[,] . . . sex, socio-economic status, smoking, sports participation, alcohol consumption, resting [systolic blood pressure], antidepressive and anxiolytic medication, . . . BMI and waist:hip ratio.” AT Ginty et al. *Depression and Anxiety are Associated with a Diagnosis of Hypertension 5 Years Later in a Cohort of Late Middle-Aged Men and Women*, 27 J. of Human Hypertension 187, 187 (2013), available at <https://www.nature.com/‌articles/‌jhh201218.pdf> (enclosed). Researchers posited that “depression and anxiety might contribute to the development of hypertension” through unhealthy behaviors and physiological dysregulation—but that the association was “still evidence after adjustment for three of the more prominent unhealthy behaviours, smoking, non participation in sports and high levels of alcohol consumption.” *Id.* at 188. A separate multivariate longitudinal analysis published in 2010 showed that “[b]oth short sleep duration and insomnia”—common symptoms of depression—“were . . . significantly associated with hypertension incidence.” James E. Gangwisch et al. *Insomnia and Sleep Duration as Mediators of the Relationship Between Depression and Hypertension Incidence*, 23 Am. J. of Hypertension 62, 62 (Jan. 2010), available at <https://‌academic.oup.com/‌ajh/‌article/‌23/‌1/‌62/‌149842?login=true> (enclosed). The researchers stated that “[d]epression has been shown to increase the risk for the development of cardiovascular disease[] in healthy subjects, and for cardiac morbidity and mortality in subjects with established cardiovascular disease.” *Id.* (footnotes omitted).

The researchers posited that sleep problems commonly caused by depression could “be mechanisms by which depression plays a role in the etiology of hypertension.” *Id.* The study found that “[a]mong middle-aged subjects, those who suffered from depression were significantly more likely . . . to have been diagnosed with hypertension over the follow-up period, and these results were attenuated with the inclusion of the covariates” of short sleep duration and insomnia. *Id.* at 66. Overall, “[m]idle-aged subjects who suffered from depression were 65% more likely to be diagnosed with hypertension over the follow-up period” and “strong arguments can be made that sleep disturbances represent a causal mechanism by which depression increases the risk for hypertension incidence.” *Id.* at 68. Another study published in 2005—a review of medical evidence from 1980 to 2004—found “considerable evidence suggesting that hyperreactivity of the sympathetic nervous system and genetic influences are the underlying mechanisms in the relationship between depression and hypertension,” and that “[d]epression can negatively affect the course of hypertensive illness” and “antidepressive agents can interfere with blood pressure control of patients with hypertension.” Andréia Zavaloni Scalco et al., *Hypertension and Depression*, 60(3) Clinics 241 (2005), available at <https://www.scielo.br/j/clin/a/‌cNrNGhMvLKxVWQSRGncXBzw/‌?format=pdf&lang=en> (enclosed).

Because this medical evidence shows a link between depression and hypertension, it is at least as likely as not that the Veteran’s service-connected depression disability or medications to treat depression caused or aggravated the current hypertension disability.

* Nexus to service-connected mental health:
  + New medical literature, AT Ginty et al. Depression and Anxiety are Associated with a Diagnosis of Hypertension 5 Years Later in a Cohort of Late Middle-Aged Men and Women, 27 J. of Human Hypertension 187, 187 (2013), available at <https://www.nature.com/‌articles/‌jhh201218.pdf>, shows a strong association between depression and anxiety and hypertension. Researchers posited that “depression and anxiety might contribute to the development of hypertension” through unhealthy behaviors and physiological dysregulation—but that the association was “still evidence after adjustment for three of the more prominent unhealthy behaviours, smoking, non participation in sports and high levels of alcohol consumption.”
  + New medical literature, Andréia Zavaloni Scalco et al., *Hypertension and Depression*, 60(3) Clinics 241 (2005), available at <https://www.scielo.br/j/clin/a/‌cNrNGhMvLKxVWQSRGncXBzw/‌?format=pdf&lang=en>, is relevant to show “considerable evidence suggesting that hyperreactivity of the sympathetic nervous system and genetic influences are the underlying mechanisms in the relationship between depression and hypertension,” and that “[d]epression can negatively affect the course of hypertensive illness” and “antidepressive agents can interfere with blood pressure control of patients with hypertension.”

Because hypertension and depression share common pathways, it is possible that each disease has an impact on the natural history of the other. Depression is common in patients with uncontrolled hypertension and may interfere with blood pressure control.

“Depression increases the risk for uncontrolled hypertension”. [Depression increases the risk for uncontrolled hypertension - PubMed (nih.gov)](https://pubmed.ncbi.nlm.nih.gov/24294029/)

#### High Blood Pressure in Service Progressed to Hypertension

Service connection for hypertension is warranted on a direct basis because the Veteran’s history of high blood pressure had its onset during service. Even if the Veteran’s blood pressure readings in service did not warrant a diagnosis of blood pressure at the time according to VA’s definition, the fact remains that the progressive increase of the Veteran’s average blood pressure readings began during service. Systolic readings of 120 to 129 are considered elevated, and hypertension is generally diagnosed—for medical if not VA purposes—where systolic pressure is 130 or greater or diastolic pressure is 80 or greater. *Understanding Blood Pressure Readings*, Am. Heart Ass’n, <https://www.heart.org/en/health-topics/high-blood-pressure/understanding-blood-pressure-readings> (last visited Oct. 13, 2022) (enclosed). Thus, every single blood pressure reading during the Veteran’s service meets the American Heart Association’s clinical definition of hypertension.

This is sufficient to meet the second element necessary for direct service connection—an in-service event, injury, or disease. The Veteran’s hypertension disease manifested during service. And although the severity of the disease did not satisfy VA’s definition of hypertension for purposes of 38 C.F.R. § 4.104 at the time, § 4.104 by its own terms does not extend beyond that section to change the definition of an in-service disease under 38 C.F.R. § 3.303. Further, the Veteran’s in-service disease is causally related to the current hypertension disability—which does satisfy VA’s definition of a disability in § 4.104—because records document progression from the Veteran’s initial elevated blood pressure in service into the service-connectable hypertension today.

#### Lead Exposure Causes Hypertension

* Nexus to lead exposure:
  + New medical literature, Ana Navas-Acien *et al.*, *Lead Exposure and Cardiovascular Disease—A Systematic Review*, 115 Env. Health Perspect. 472 (2006), is relevant to show that “Chronic lead poisoning was connected to hypertension in the 19th century.” The review documents centuries of medical research connecting lead exposure to hypertension and other cardiovascular conditions. The researchers “conclude that the evidence is sufficient to infer a causal relationship between lead exposure and high blood pressure.”

#### Obesity Causes Hypertension

The medical “relationship between obesity and hypertension is well established.” Vasilios Kotsis et al., *Mechanisms of Obesity-Induced Hypertension*, 33 Hypertension Research 386, 386 (2010) (enclosed). And although there is still more research to be done about how precisely obesity causes hypertension, the causal relationship—not just an association—is recognized by researchers. *See generally id.* There is evidence that obesity causes hypertension through activation of the sympathetic nervous system, renal mechanisms, hormonal changes, endothelial dysfunction, and changes in vascular structure. *Id.*

* + New medical article, Vasilios Kotsis et al., *Mechanisms of Obesity-Induced Hypertension*, 33 Hypertension Research 386 (2010), is relevant to show that the medical causal “relationship between obesity and hypertension is well established.”

#### Obstructive Sleep Apnea Causes Hypertension

In 2018, researchers published a meta-analysis of studies showing an association between obstructive sleep apnea (OSA) and hypertension showing significant evidence that OSA is a risk factor for hypertension. Haifeng Hou et al., *Association of Obstructive Sleep Apnea with Hypertension: A Systematic Review & Meta-Analysis*, 8 J. of Global Health 010405 (June 2018) (enclosed). The meta-analysis drew data from 26 published studies including 4 prospective cohort studies and 21 case-control studies involving a total of more than 51,000 participants. *Id.* “The synthesized results showed that OSA was significantly associated with resistant hrn with a pooled OR of 2.842 . . . which indicated that OSA participants had an extra 1.842-fold risk for resistant hypertension.” *Id.* Additional meta-analysis showed that even “essential hypertension was significantly associated with OSA” with ORs ranging from 1.093 to 1.561 depending on OSA severity (“the more serious OSA is, the higher hypertension risk occurs”). *Id.*

* Nexus to service-connected sleep apnea:
  + New medical literature, Haifeng Hou et al., *Association of Obstructive Sleep Apnea with Hypertension: A Systematic Review & Meta-Analysis*, 8 J. of Global Health 010405 (June 2018), is relevant to show “that OSA was significantly associated with resistant hrn with a pooled OR of 2.842 . . . which indicated that OSA participants had an extra 1.842-fold risk for resistant hypertension.” Additional meta-analysis showed that even “essential hypertension was significantly associated with OSA” with ORs ranging from 1.093 to 1.561 depending on OSA severity (“the more serious OSA is, the higher hypertension risk occurs”).

#### Posttraumatic Stress Disorder (PTSD) Causes Hypertension

In a 2017 study reviewing the VA health records of nearly 200,000 OIF/OEF/OND veterans with PTSD, 27 percent had blood pressure readings in the hypertensive range and 10 percent were diagnosed as having hypertension. Matthew M. Burg et al., *Risk for Incident Hypertension Associated with PTSD in Military Veterans, & the Effect of PTSD Treatment*, 79 Psychosom Med. 181–88 (2017) (enclosed). Overall, untreated PTSD “was associated with a 24–46% greater risk of incident hypertension.” *Id.* The researchers explained that PTSD causes “dysregulation in hypothalamic pituitary-adrenocortical and sympathetic-adrenal-medullary stress axes. Ongoing dysregulation in these pathways can disrupt regulation of BP, inflammation, and associated gene expression.” *Id.* (footnotes omitted). In sum, the study found prospective increased risk of hypertension ***attributable to PTSD***, which was worsened when PTSD went untreated. *Id.*

* + New medical article, Matthew M. Burg et al., *Risk for Incident Hypertension Associated with PTSD in Military Veterans, & the Effect of PTSD Treatment*, 79 Psychosom Med. 181–88 (2017), is relevant to show that PTSD causes “dysregulation in hypothalamic pituitary-adrenocortical and sympathetic-adrenal-medullary stress axes. Ongoing dysregulation in these pathways can disrupt regulation of BP, inflammation, and associated gene expression.”

#### Prostate Cancer Causes Hypertension

## Ischemic Heart Disease

#### Migraine Associated with Ischemic Heart Disease

* + New medical literature, Aisha Saeed et al., *Association of Migraine and Ischemic Heart Disease: A Review*, 11 Cureus e5710 (2019), available at <https://pubmed.ncbi.nlm.nih.gov/31720187/>, is relevant to show that migraines and IHD are strongly associated through multiple potential mechanisms.

# Digestive

#### Functional Gastrointestinal Disorders (MUCMIs) in Jordan

Veterans with qualifying service in the Southwest Asia theater of operations are entitled to presumptive service connection for objective indications of a disability resulting from (1) an undiagnosed illness, or (2) a medically unexplained chronic multisymptom illness (MUCMI) that is defined by a cluster of signs or symptoms. 38 C.F.R. § 3.317(a). Service connection ***must be granted*** for either an undiagnosed illness or a MUCMI became manifest during active service in the Southwest Asia theater of operations or to a degree of 10 percent or more not later than December 31, 2026.

A MUCMI is a diagnosed illness without conclusive pathophysiology or etiology such as chronic fatigue syndrome, fibromyalgia, or functional gastrointestinal disorders. Irritable bowel syndrome (IBS), which the Veteran is diagnosed as having per a binding favorable factual finding, is a MUCMI. 38 C.F.R. § 3.317, Note to paragraph (a)(2)(i)(B)(3).

The Veteran admittedly does not have service in the Southwest Asia theater of operations. However, he does have multiple periods of service in Jordan, just 30 miles from the border with Saudi Arabia—which is within the Southwest Asia theater of operations.

Environmental exposures are not cognizant of national boundaries. The hazards that cause Gulf War Illness—although presumed only in the areas listed above—also exist outside the Southwest Asia theater of operations, particularly just 30 miles from the geographical boundary.

Evidence enclosed here supports that functional gastrointestinal disorders—which are MUCMIs—are also prevalent in Jordan. A study of school children in Jordan based on 1,587 returned questionnaires found that 32.4 percent had functional gastrointestinal disorders, and a whopping 40 percent in children 11 to 18 years of age. Eyad Altamimi, *National Prevalence of Functional Gastrointestinal Disorders in Jordanian Children*, 13 Clin. & Exper. Gastro. 267 (2020), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC7423213/‌pdf/ceg-13-267.pdf> (enclosed). This represents a much more widespread problem than in other countries recently studied, such as in Ecuador (22.8%), Sri Lanka (28.7%), or Egypt (25.7%). *Id.* at 270.

This evidence supports the prevalence of MUCMIs like the Veteran’s in Jordan, even though Jordan is not included in the presumptive area. Based on this information, it is at least as likely as not that the Veteran was exposed to environmental hazards that VA has acknowledged as causative factors of disabilities including IBS.

#### Gastrointestinal Problems Associated with War

Gastrointestinal problems are common during wars, and they have exerted significant adverse effects on the health of service members involved in warfare. The risk to military personnel for digestive diseases has increased.

“Gastrointestinal problems in modern wars”. [Gastrointestinal problems in modern wars: clinical features and possible mechanisms - PubMed (nih.gov)](https://pubmed.ncbi.nlm.nih.gov/26301101/#:~:text=Data%20revealed%20that%20gastrointestinal%20symptoms,military%20personnel%20during%20modern%20wars.)

#### NSAIDs Cause Gastrointestinal Issues

Nonsteroidal anti-inflammatory drugs, including ibuprofen, are widely known to cause upper gastrointestinal problems. Carlos Sostres et al., *Nonsteroidal Anti-Inflammatory Drugs and Upper and Lower Gastrointestinal Mucosal Damage*, 15 Arthritis Research & Therapy Suppl. 3 (2013) (enclosed). “The most important upper GI side effects are the occurrence of symptomatic and/or complicated peptic ulcer. NSAID-related upper GI complications include bleeding, perforation and obstruction.” *Id.* Studies show that NSAID users have four or five times the relative risk of developing peptic ulcers compared with nonusers. *Id.* “A number of reports have suggested that NSAIDs also cause lower GI tract injury and complications.” *Id.*

* Nexus to painful service-connected disabilities through NSAID use:
  + New medical article, Carlos Sostres et al., *Nonsteroidal Anti-Inflammatory Drugs and Upper and Lower Gastrointestinal Mucosal Damage*, 15 Arthritis Research & Therapy Suppl. 3 (2013), is relevant to show that “The most important upper GI side effects are the occurrence of symptomatic and/or complicated peptic ulcer. NSAID-related upper GI complications include bleeding, perforation and obstruction.”

## Acid Reflux

#### Posttraumatic Stress Disorder (PTSD) Causes Acid Reflux

One study showed that Veterans with PTSD had double the chance of suffering from acid reflux.

“The gut reaction to PTSD”. [The gut reaction to PTSD – Gallipoli (gallipoliresearch.com.au)](https://www.gallipoliresearch.com.au/2017/03/20/the-gut-reaction-to-ptsd/)

## Gastroesophageal Reflux Disease (GERD)

#### Depression Causes GERD

The Veteran is entitled to service connection for GERD because medical research shows that depression, for which the Veteran is in receipt of service connection, causes or aggravates GERD.

In 2018, researchers conducted two nested case-control studies, one comparing nearly 61,000 participants with depression to more than 240,000 control participants, and a second study comparing over 133,000 participants with GERD to more than 266,000 participants without. So Young Kim et al., *Bidirectional Association Between Gastroesophageal Reflux Disease and Depression: Two Different Nested Case-Control Studies Using a National Sample Cohort*, 8:11748 Nature Scientific Reps. (2018) at 1, <https://www.nature.com/articles/s41598-018-29629-7.pdf> (enclosed). The rate of GERD in the depression group was 16.3 percent compared with 9 percent in the control, and the rate of depression in the GERD group was 5.7 percent versus 3.9 percent in the control. *Id.* at 2. The results were consistent across all age and gender groups. *Id.*

The researchers offered multiple well-reasoned explanations for this association—including theories that depression may cause or aggravate GERD:

Depression might also increase the risk of GERD. First, the fear of reflux symptoms might increase the individual’s perception of reflux symptoms[]. Psychological factors could reduce the sensation threshold in the body[] and increase the sensation of esophageal stimulation24. Second, depression might actually increase reflux. Psychological factors can decrease the pressure of the lower esophageal sphincter[], change esophageal motility[], increase gastric acid secretion[], and decrease acid clearance in the esophagus[]. Third, antidepressant medication might aggravate refux[]. Anticholinergic drugs may lower the pressure of the lower esophageal sphincter[]. Moreover, drugs have been shown to delay gastric emptying, inhibit esophageal peristalsis, and decrease salivary secretion[].

Furthermore, confounders such as obesity, eating habits, smoking, alcohol drinking, lack of sleep, and high stress might aggravate both GERD and depression[]. Stress induces GERD[] and promotes depression[].

*Id.* (footnotes omitted).

These concerns were echoed in a 2019 cross-sectional study of 258 patients with GERD, among whom 41.4 percent had depression, 34.4 percent had anxiety, and 27.13 percent had both. Saleh Mohammed Channa, *Depression and Anxiety in Patients with and Without Chest Pain*, 11(11) Cureus e6103, 1 (Nov. 8, 2019), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC6858267/pdf/cureus-0011-00000006103.pdf> (enclosed). The researchers explained that “[s]tress and emotions can alter GI function and can even cause GI symptoms and disease. . . . Psychological factors may affect the severity of a GI disorder by affecting the perception of pain through the gut-brain axis.” *Id.* Moreover, it has been shown that “the treatment of GERD in the presence of psychological effects can become hindered” *Id.* at 4.

Given the statistical increase in risk for GERD among depression patients, and the equally plausible theories that depression causes or aggravates GERD, the evidence of record is at least in relative equipoise and the Veteran is entitled to service connection for GERD on a secondary basis.

* Nexus to service-connected depression:
  + New medical article, So Young Kim et al., *Bidirectional Association Between Gastroesophageal Reflux Disease and Depression: Two Different Nested Case-Control Studies Using a National Sample Cohort*, 8:11748 Nature Scientific Reps. (2018), <https://www.nature.com/articles/s41598-018-29629-7.pdf>, is relevant to show that:

Depression might also increase the risk of GERD. First, the fear of reflux symptoms might increase the individual’s perception of reflux symptoms[]. Psychological factors could reduce the sensation threshold in the body[] and increase the sensation of esophageal stimulation24. Second, depression might actually increase reflux. Psychological factors can decrease the pressure of the lower esophageal sphincter[], change esophageal motility[], increase gastric acid secretion[], and decrease acid clearance in the esophagus[]. Third, antidepressant medication might aggravate refux[]. Anticholinergic drugs may lower the pressure of the lower esophageal sphincter[]. Moreover, drugs have been shown to delay gastric emptying, inhibit esophageal peristalsis, and decrease salivary secretion[].

Furthermore, confounders such as obesity, eating habits, smoking, alcohol drinking, lack of sleep, and high stress might aggravate both GERD and depression[]. Stress induces GERD[] and promotes depression[].

* + New article, Saleh Mohammed Channa, *Depression and Anxiety in Patients with and Without Chest Pain*, 11(11) Cureus e6103, (Nov. 8, 2019), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC6858267/pdf/cureus-0011-00000006103.pdf>, is relevant to show that “[s]tress and emotions can alter GI function and can even cause GI symptoms and disease. . . . Psychological factors may affect the severity of a GI disorder by affecting the perception of pain through the gut-brain axis.”

#### Drinking Causes or Aggravates GERD

Most research on the topic shows that “heavy drinking puts people at high risk for many adverse health events, potentially including GERD. Alcohol consumption may increase symptoms of GERD and cause damage to the esophageal mucosa.” Shao-hua Chen et al., *Is Alcohol Consumption Associated with Gastroesophageal Reflux Disease?*, 11 Biomed & Biotechnical 423–28, 423 (2010), available at https://‌www.‌ncbi.‌nlm.‌nih.‌gov/‌pmc/‌articles/‌PMC2880354/pdf/JZUSB11-0423.pdf.

#### IBS Associated with GERD

The Veteran’s current GERD disability is at least as likely as not caused by or aggravated by his service-connected irritable bowel syndrome (IBS) disability.

In a 2010 study of over 6,000 patients with gastrointestinal dysfunction, researchers found that among IBS subjects, 63.6 percent also had GERD, compared with only 34.7 percent of those without IBS. Shadi Sadeghi Yarandi et al. *Overlapping Gastroesophageal Reflux Disease and Irritable Bowel Syndrome: Increased Dysfunctional Symptoms*, 16 World J. of Gastroenterology 1232, 1232 (Mar. 14, 2010), https://www.ncbi.nlm.nih.gov/pmc/articles/‌PMC2839176/‌pdf/‌WJG-‌16-‌1232.pdf. Similarly, a 2006 systematic review of 15 studies between 1966 and 2005 suggested a causal relationship between the two conditions:

IBS and GERD appear to overlap to a degree that is greater than their individual prevalence in the community. Furthermore, the data show that each condition is less prevalent in the community if the other is excluded from the analysis. This suggests a possible causal relationship.

*Id.* at 2118. Given the decades-worth of data, it is at least as likely as not that IBS causes or aggravates GERD.

#### Obesity Causes GERD

Multiple medical studies have shown a strong association between obesity and long-term complications of GERD, such as erosive esophagus. Paul Chang and Frank Friedenberg, *Obesity & GERD*, 43 Gastroenterol Clin. N. Am. 161 (2014), available at <https://www.ncbi.nlm.nih.gov/‌pmc/articles/PMC3920303/pdf/nihms-552827.pdf> (enclosed). “Several physiologic abnormalities which could lead to prolonged esophageal acid exposure have been found to occur more frequently in obese compared to normal weight individuals.” *Id.* There are multiple theories for the pathophysiological relationship between the two conditions, including increases to intra-abdominal pressure in obese patients, or decreased secretion of adiponectin due to obesity. *Id.* Further, studies have “found that weight loss was dose-dependently associated with a reduction of symptoms.” *Id.*

* + New medical article, Paul Chang and Frank Friedenberg, *Obesity & GERD*, 43 Gastroenterol Clin. N. Am. 161 (2014), available at <https://www.ncbi.nlm.nih.gov/‌pmc/articles/PMC3920303/pdf/nihms-552827.pdf>, is relevant to show that “Several physiologic abnormalities which could lead to prolonged esophageal acid exposure have been found to occur more frequently in obese compared to normal weight individuals.”

#### Obstructive Sleep Apnea (OSA) Causes GERD

“It sounds plausible that sympathetic nerve dominance could potentially associate IBS and sleep apnea. To elaborate, hypoxia induces activation of sympathetic nervous system, which provides critical levels of oxygen being indispensable for physiological function.” [Association of irritable bowel syndrome and sleep apnea in patients referred to sleep laboratory (nih.gov)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5508502/)

#### PTSD Causes GERD

A retrospective chart review of VA charts revealed that of patients with gastrointestinal symptoms, 73.4 percent of them had positive PTSD screens. Laila Menon, *PTSD, Depression, and Gastrointestinal Symptoms in Veterans of the Afghanistan and Iraq Conflicts: What’s the Relation?*, 108 Am. J. of Gastroenterology S571 (Oct. 2013) (enclosed). According to the researchers, “positive screening of PTSD was significantly associated with . . . GI symptoms” including GERD (with an OR of 4.6). *Id.* And a broader cohort study of over 4,000 Danish patients with history of PTSD “found that PTSD was associated with most individual GI disorders.” Jaimie L. Gradus, *Posttraumatic Stress Disorder and Gastrointestinal Disorders in the Danish Population*, 28 Epidemiology 354 (May 2017), available at <https://www.ncbi.nlm.‌nih.‌gov/‌‌pmc/‌articles/‌PMC5523445/‌pdf/‌‌nihms866996.pdf> (enclosed).

* Nexus to service-connected PTSD:
  + New medical article, Laila Menon, *PTSD, Depression, and Gastrointestinal Symptoms in Veterans of the Afghanistan and Iraq Conflicts: What’s the Relation?*, 108 Am. J. of Gastroenterology S571 (Oct. 2013), is relevant to show that “positive screening of PTSD was significantly associated with . . . GI symptoms” including GERD (with an OR of 4.6).
  + New medical article, Jaimie L. Gradus, *Posttraumatic Stress Disorder and Gastrointestinal Disorders in the Danish Population*, 28 Epidemiology 354 (May 2017), available at <https://www.ncbi.nlm.‌nih.‌gov/‌‌pmc/‌articles/‌PMC5523445/‌pdf/‌‌nihms866996.pdf>, a cohort study of over 4,000 Danish patients with history of PTSD, which “found that PTSD was associated with most individual GI disorders.”

#### Sertraline Causes Heartburn or Indigestion

Sertraline is known to cause side effects such as indegestion and heartburn. Mayo Clinic (last updated May 1, 2024), <https://www.mayoclinic.org/drugs-supplements/sertraline-oral-route/side-effects/drg-20065940>. And if it becomes chronic, acid reflux or heartburn symptoms can progress into GERD and cause additional complications. *What’s the Difference? Heartburn vs. Acid Reflux vs. GERD*, CrozerHealth (May 30, 2017), https://www.crozerhealth.org/news/news-releases/‌2017/‌heres-how-to-understand-the-difference-between-heartburn-acid-reflux-and-gerd-and-what-you-can-do-to-if-you-have-any-of-these-conditions/.

Because of these known causal relationships between sertraline—which the Veteran takes for service-connected disability—and GERD, the evidence of record is at least in relative equipoise and the Veteran is entitled to service connection for GERD on a secondary basis.

## Hemorrhoids

#### Irritable Bowel Syndrome Causes or Aggravates Hemorrhoids

The Veteran is entitled to service connection for the current hemorrhoid disability because medical research shows that hemorrhoids are caused by or aggravated by IBS.

In a 2009 study comparing patients with irritable bowel syndrome (IBS) to those without, researchers found that hemorrhoids were detected in 33.3 percent of IBS patients, but only 15.7 percent of those without IBS. Mehmet Rami Helvaci et al., *Irritable Bowel Syndrome and Chronic Gastritis, Hemorrhoid, Urolithiasis*, 41 Eurasian J. of Med. 158, 158 (Dec. 2009), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4261279/pdf/eajm-41-3-158.pdf. The researchers concluded that the relationship was significant, and “[e]xcessive straining, feeling of incomplete evacuation, repeated toilet visits, and periods of constipation are . . . found among the possible causes of [hemorrhoids] in IBS cases.” *Id.* at 161.

Because this medical evidence establishes a significant relationship between IBS and hemorrhoids, it is at least as likely as not that the Veteran’s service-connected IBS disability caused or aggravated the current hemorrhoid disability.

## Irritable Bowel Syndrome

#### GERD Associated with IBS

In a 2010 study of over 6,000 patients with gastrointestinal dysfunction, researchers found that among IBS subjects, 63.6 percent also had GERD, compared with only 34.7 percent of those without IBS. Shadi Sadeghi Yarandi et al. *Overlapping Gastroesophageal Reflux Disease and Irritable Bowel Syndrome: Increased Dysfunctional Symptoms*, 16 World J. of Gastroenterology 1232, 1232 (Mar. 14, 2010), https://www.ncbi.nlm.nih.gov/pmc/articles/‌PMC2839176/‌pdf/‌WJG-‌16-‌1232.pdf. Similarly, a 2006 systematic review of 15 studies between 1966 and 2005 suggested a causal relationship between the two conditions:

IBS and GERD appear to overlap to a degree that is greater than their individual prevalence in the community. Furthermore, the data show that each condition is less prevalent in the community if the other is excluded from the analysis. This suggests a possible causal relationship.

*Id.* at 2118. Given the decades-worth of data, it is at least as likely as not that GERD causes or aggravates IBS.

# Genitourinary

## Sexual Dysfunction

#### Anxiety Causes Erectile Dysfunction

A 2022 medical study demonstrates “high prevalence of ED in the anxiety disorder population and ED may be more severe in this cohort.” Rajalaxmi Velurajah et al., *Erectile Dysfunction in Patients with Anxiety Disorders: A Systematic Review*, 34 Your Sexual Med. J. 177, 177 (2022), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8964411/> (enclosed). Studies note the prevalence of risk factors for ED among patients with anxiety disorders, including “the use of psychotropic drugs such as selective serotonin reuptake inhibitors. It has been shown that antidepressants like these may cause 30 to 40% of patients to develop sexual dysfunction.” *Id.* at 182 (citations omitted).

* Nexus to service-connected anxiety:
  + New medical literature, Rajalaxmi Velurajah et al., *Erectile Dysfunction in Patients with Anxiety Disorders: A Systematic Review*, 34 Your Sexual Med. J. 177, 177 (2022), available at [https://www.ncbi.nlm.nih.gov/pmc/articles/‌PMC8964411/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8964411/), is relevant to show a “high prevalence of ED in the anxiety disorder population and ED may be more severe in this cohort.”

#### Coronary Artery Disease Causes Erectile Dysfunction

Well-founded medical research shows that “[a]rtherosclerosis can play a major role in the development of ED.” Sai Ravi Shanker et al., *Association Between Erectile Dysfunction and Coronary Artery Disease and It’s Severity*, 65 Ind. Heart J. 180, 181 (2012), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3861235/> (enclosed). The relationship is particularly significant among patients with diabetes. *Id.* And evidence shows “that rather than being a disease of the penile vasculature, ED may be a manifestation of a systemic vascular disease.” Rohit Kapoor and Aditya Kapoor, *Erectile Dysfunction: A Present Day Coronary Disease Risk Equivalent*, 144 Ind. J. Med. Res. 307, 307 (2016), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5320833/> (enclosed).The correlation between these conditions is so strong, in fact, that ED is often used as a risk factor to identify early stages of coronary artery disease “[s]ince symptoms of ED often appeare before that of CAD due to the smaller size of the penile vasculature.” *Id.*

#### Depression Causes Erectile Dysfunction

There is a clear association between depression and ED as supported by a large number of recent studies of the phenomenon. *See generally*, Qian Liu et al., *Erectile Dysfunction & Depression: A Systematic Review & Meta-Analysis*, 15 J. Sex. Med. 1073–82 (2018) (enclosed).

* Nexus to service-connected depression:
  + New medical literature, Qian Liu et al., *Erectile Dysfunction & Depression: A Systematic Review & Meta-Analysis*, 15 J. Sex. Med. 1073 (2018), is relevant to show that a large number of studies support a clear association between depression and ED.

#### Epilepsy/Anti-Epilepsy Medication Causes Erectile Dysfunction

Medical research has “clearly demonstrated that patients with different types of neurological disorders have a higher risk to develop sexual dysfunction than the general population.” Eva Hellmis, *Sexual Problems in Males with Epilepsy—An Interdisciplinary Challenge!*, 17 Seizure 139–40, 136 (2008). “Up to 60% of the male patients with epilepsy are affected by sexual function disorders,” compared with approximately 20–22% of the general male population worldwide. *Id.* at 136, 137. “The reasons for developing sexual dysfunction: among patients with epilepsy “are multi-factorial. Some of the symptoms are caused by the epilepsy itself while others may be caused by the antiepileptic medication.” *Id.* at 137.

#### Hypertension Causes Erectile Dysfunction

* Nexus to service-connected hypertension:
  + New medical literature, Valter Javaroni & Mario Fritsch Neves, *Erectile Dysfunction and Hypertension: Impact on Cardiovascular Risk and Treatment*, Int. J. Hypertension 627278 (2012), available at <https://pmc.ncbi.nlm.nih.gov/articles/PMC3357516/>, is relevant to show “that the main reason for ED among hypertensive individuals were penile circulation disability (found in 89%), probably due to atherosclerosis.”

#### Obesity Causes Erectile Dysfunction

Obesity is a proven independent risk factor for ED in men, with “79% of men presenting erectile disorders hav[ing] BMI of 25 lg/m2 or greater.” Damian Skrypnik *et al.*, *Obesity—Significant Risk Factor for Erectile Dysfunction in Men*, 38 Pol. Merkur Lekarski 137 (2014), available at <https://pubmed.ncbi.nlm.nih.gov/24720114/> (abstract enclosed). The independent risk of ED scales up for a greater chance of ED the higher the BMI. *Id.* In fact, “[o]besity leads to erectile dysfunction in a considerably greater extent than aging. Mechanisms responsible for the independent influence of obesity on the erectile dysfunction are: hormonal imbalance, endothelial dysfunction, insulin resistance, psychological factors and physical inactivity.” *Id.*

#### Pain Causes Sexual Dysfunction

* Nexus to service-connected painful disabilities:
  + New medical literature, Lindsay G. Flegge et al., *Sexual Functioning Among Adults with Chronic Pain: Prevalence and Association with Pain-Related Outcomes*, 24 Pain Med. 197 (2023), is relevant to show that “patients with chronic pain experience significant sexual dysfunction, including lack of interest in sexual activity and low satisfaction with their sex lives.”

#### PTSD Causes Sexual Dysfunction

The Veteran is entitled to secondary service connection for ED. He is currently in receipt of service connection for posttraumatic stress disorder (PTSD). VA’s own analysis of current medical research confirms that “male Veterans with PTSD were significantly more likely than their civilian counterparts to report erectile dysfunction or other sexual problems.” *Sexual Dysfunction a Common Problem in Veterans with PTSD*, VA Journal Scan, <https://www.research.va.gov/‌currents/‌spring2015/‌spring2015-3.cfm> (Mar. 24, 2015) (enclosed). “PTSD impairs sexual functioning across multiple domains: desire, arousal, orgasm, activity, and satisfaction.” *Id.*

In one study, of male combat Veterans diagnosed with PTSD, for example, 85 percent reported erectile dysfunction, compared with a 22 percent rate among male combat Veterans without any mental health diagnosis. Another study of 90 male combat Veterans with PTSD found more than 80 percent were experiencing sexual dysfunction.

Thus, it is at least as likely as not that the Veteran’s ED is caused by his service-connected PTSD and service connection is warranted.

* + New medical article, *Sexual Dysfunction a Common Problem in Veterans with PTSD*, VA Journal Scan, <https://www.research.va.gov/‌currents/‌spring2015/‌spring2015-3.cfm> (Mar. 24, 2015), is relevant to show that “male Veterans with PTSD were significantly more likely than their civilian counterparts to report erectile dysfunction or other sexual problems.”

#### Traumatic Brain Injury (TBI) Causes Erectile Dysfunction

In a 2018 population study that compared over 72,000 patients with TBI to over 217,000 patients without TBI, researchers found that “patients with TBI have a significantly higher risk of developing ED.” Yun-Ju Yang et al., *Traumatic Brain Injury: A Nationwide Population-Based Cohort Study in Taiwan*, 12 Am. J. of Men’s Health 913, 913 (2018), <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC6131467/‌pdf/‌10.1177_1557988317750970.pdf> (enclosed). Among the population with TBI, the risk of ED was 24.66 in 100,000, while the risk among those without TBI was only 19.07. *Id.* Other sources suggest the risk for ED among men with TBI is between 40 and 60 percent. *Brain Injury and Sexual Issues*, BetterHealth Channel, <https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/brain-injury-and-sexual-issues> (last visited Sept. 11, 2021) (enclosed). Sexual dysfunction after TBI can be caused by damage to parts of the brain controlling sexual function, hormonal changes, medication side effects, fatigue, problems with physical movement, self-esteem problems, changes in cognitive function, emotional changes, or changes in ability to create and maintain relationships. *Sexuality After Traumatic Brain Injury*, TBI Model Sys. & U. Wash. Model Sys. Knowledge Translation Ctr. (2011), <https://msktc.org/‌sites/‌default/‌files/‌TBI_‌Sexuality%20and%20TBI.pdf> (enclosed).

* Nexus to service-connected TBI:
  + New medical literature, Yun-Ju Yang et al., *Traumatic Brain Injury: A Nationwide Population-Based Cohort Study in Taiwan*, 12 Am. J. of Men’s Health 913 (2018), available at <https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC6131467/‌pdf/‌10.1177_1557988317750970.pdf>, is relevant to show that patients with TBI have a significantly higher risk of developing ED.”
  + New medical literature, *Sexuality After Traumatic Brain Injury*, TBI Model Sys. & U. Wash. Model Sys. Knowledge Translation Ctr. (2011), <https://msktc.org/‌sites/‌default/‌files/‌TBI_‌Sexuality%20and%20TBI.pdf>, is relevant to show that sexual dysfunction after TBI can be caused by damage to parts of the brain controlling sexual function, hormonal changes, medication side effects, fatigue, problems with physical movement, self-esteem problems, changes in cognitive function, emotional changes, or changes in ability to create and maintain relationships.

## Kidneys

#### Onset of Chronic Kidney Disease

Medical treatise evidence shows that early stage chronic kidney disease does not tend to show symptoms and goes undetected unless specific tests are run to identify it. *Symptoms Chronic Kidney Disease*, NHS (Aug. 29, 2019), https://www.nhs.uk/conditions/kidney-disease/symptoms/. The Veteran did not undergo any of these tests during service or upon separation. Therefore, it is at least as likely as not that the Veteran’s current chronic kidney disease actually began during service, but did not progress enough to be identified until after service.

#### Herbicide Agents Cause Kidney Disabilities

Medical research supports a finding that the Veteran’s current kidney disability is at least as likely as not caused by exposure to herbicide agents. “A hospitalization study of New Zealand Vietnam veterans found that chronic renal failure risk was statistically significantly increased among the veterans compared with the standardized general population of New Zealand.” Nat’l Acads. of Scis. Eng’g Med., Veterans and Agent Orange: Update11 540 (2018). And one “environmental exposure study of Taiwanese residents living in close proximity to a former PCP-producing factory found that those who had high serum dioxin levels had a statistically significantly elevated risk of chronic kidney disease.” *Id.*

Although the National Academy of Sciences has stated that there is not enough evidence to conclude that exposure to herbicide agents causes kidney disabilities as a medical certainty, the medical treatise evidence above provides Hypertension Causes or Aggravates Chronic Kidney Disease

The Veteran is currently in receipt of service connection for hypertension. Medical treatise evidence shows that “[h]igh blood pressure is a leading cause of” chronic kidney disease. Nat’l Kidney Found., High Blood Pressure and Chronic Kidney Disease 7 (2010), available at <https://www.kidney.org/sites/default/‌files/‌docs/‌hbpandckd.pdf> (enclosed). And hypertension aggravates the progression of chronic kidney disease. *Id.* This relationship is well established—having been identified in the 19th century. Elsa Morgado & Pedro Leāo Neves, *Hypertension and Chronic Kidney Disease: Cause and Consequence – Therapeutic Considerations*, *in* Antihepertensive Drugs II 45, 45 (Hossein Babaei, ed., 2012), available at <https://www.intechopen.com/chapters/34159> (enclosed).

Given this medical evidence of a well-established nexus between hypertension and chronic kidney disease, the evidence of record is at least in relative equipoise as to whether it is at least as likely as not that the Veteran’s service-connected hypertension caused or aggravated the current kidney disability and service connection must be granted.

#### PFAS Causes Kidney Cancer

*Guidance on PFAS Exposure, Testing, and Clinical Follow-Up 2022*, Nat’l Acads. Scis. Comm. on Guidance on PFAS Testing & Health Outcomes (2022), available at <https://nap.naptionalacademies.org/26156> (enclosed).

#### PTSD Causes or Aggravates Chronic Kidney Disease

A population-matched cohort study including nearly 31,000 participants showed that stress-related disorders are associated with increased risk of subsequent progression of chronic kidney disease. Guobin Su *et al.*, *Stress Related Disorders and the Risk of Kidney Disease*, 6 Kidney Int’l Reps. 706 (2021), available at <https://www.sciencedirect.com/science/‌article/‌pii/‌S2468024920318660> (enclosed). “This study thus identifies SRDs as a novel and plausible risk factor for kidney damage, both acute and chronic, in the community.” *Id.* at 710. Although the studies on this topic are so far only observational, the researchers identified medically plausible mechanisms for causation or aggravation—which is enough to satisfy the low burden of proof of a nexus for secondary service connection; for example:

psychological stress induces changes in cortisol, enhances the sympathetic nervous system activity and results in sodium/water retention. Stress also impairs insulin sensitivity, while promotes metabolic syndrome and diabetes by altering the hypothalamic-pituitary-adrenal axis (via increased glucocorticoid and other stress hormones). Stress also increases the risk of autoimmune diseases through impairments of immune function and enhanced inflammatory reactivity. Finally, stress induces tissue ischemia and hemodynamic changes which may accelerate the onset of AKI.

*Id.* at 711–12 (footnotes omitted).

## Prostate Cancer

#### Agent Orange Causes Prostate Cancer

There is medical research showing a plausible causative association between exposure to 2,3,7,8-tetrachlorodibezo-p-dioxin (TCDD, the herbicide agent in Agent Orange) and the development of prostate cancer. A meta-analysis of 17 cohort studies showed an overall standardized mortality ratio of 1.26 and risk ratio of 1.04. L. Leng et al., *2,3,7,8-Tetrachlorodibezo-P-Dioxin Exposure & Prostate Cancer: A Meta-Analysis of Cohort Studies*, 128 Pub. Health 207–213 (2014). The researchers explained several ways in which TCDD exposure causes prostate cancer:

Some animal studies indicated that TCDD acts directly on Aryl hydrocarbon Receptor (AhR), Aryl hydrocarbon Receptor Nuclear Translocator (ARNT), and AhR-induced transcripts in the periprostatic mesenchyme, and disrupts the dorsoventral patterning of the urogenital sinus. As a result, the prostatic bud areas are reprogrammed, and the formation of the prostate lobes is disrupted. In addition, TCDD has been shown to induce cytochrome P450, family 1, subfamily A, polypeptide 1 (CYP1A1) activity and to a lesser extent cytochrome P450, family 1, subfamily B (CYP1B) activity in the hormoneindependent human prostate cancer cell lines. It also dramatically induces cytochrome P450, family 1, subfamily A, polypeptide 2 (CYP1A2) mRNA expression. Moreover, TCDD exposure induces matrix metalloproteinase 9 (MMP-9) expression in human prostate cancer cells, suggesting that TCDD may regulate the expression of genes involved in tumour invasion.

*Id.* at 211. Overall, the researchers concluded the data “suggests that TCDD exposure is a contributing risk factor for prostate cancer” along with the traditional risk factors of age genetic predisposition, and endocrine factors. *Id.* at 210, 212.

#### Asbestos Causes Prostate Cancer

In a 2020 meta-analysis of 33 studies, researchers found that “[b]oth environmental and occupational asbestos exposure were linked to increased risk of prostate cancer” with an effect size of 1.25. Frédéric Dutheil et al., *Prostate Cancer and Asbestos: A Systematic Review and Meta-Analysis*, 24 Permanente J. 19.086, 1 (Feb. 14, 2020), https://doi.org/‌10.7812/‌TPP/‌19.086.

# Gynecological Conditions and Disorders of the Breast

# Hematologic and Lymphatic Systems

## Multiple Myeloma

#### PFOA/PFOS Causes Multiple Myeloma

The second element for service connection—an in-service injury—is shown by new and relevant evidence. The government reports enclosed show toxic contamination of perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) in the drinking and groundwater at several military installations where the Veteran served, including Fort Drum and Soto Cano Air Base.

Currently, the EPA has in place a health advisory of 70 parts per trillion in drinking water. EPA, *Drinking Water Health Advisories for PFOA and PFOS*, <https://www.epa.gov/‌ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos> (last visited mar 25, 2022) (enclosed). In June 2016 a Department of Defense (DoD) investigation revealed 36 drinking-water systems with PFOS/PFOA levels above 70 parts per trillion. In addition, testing of groundwater near 401 DoD installations found 90 with contamination levels above 70 parts per trillion.

DoD installations with PFOA/PFOS contamination in ground- or drinking-water above 70 parts per trillion include Soto Cano Air Base and Fort Drum, where the Veteran was stationed—with contamination levels up to 82.9 and a ***whopping 15,000 parts per trillion***, respectively. Maureen Sullivan, Deputy Assistant Secretary of Defense (Environment, Safety & Occupational Health), *Addressing Perfluorooctane Sulfonate (PFOS) & Perfluorooctanoic Acid (PFOA)* (Mar. 2018) 21, 25, available at <https://partner-mco-archive.s3.‌amazonaws.‌com/‌client_files/‌1524589484.pdf?_ga=2.112630087.2134173778.1648233477-685478305.‌1648233477> (enclosed).

Finally, the third element for service connection is shown by additional new and relevant evidence. As the Veteran’s enclosed statement supports, he has no other risk factors for developing multiple myeloma (*see also Risk Factors for Multiple Myeloma*, American Cancer Society, <https://www.cancer.org/cancer/multiple-myeloma/causes-risks-prevention/risk-factors.html> (last revised Feb. 28, 2018) (enclosed). The only remaining risk factor identifiable in the Veteran’s case is his more than likely exposure to incredibly high levels of PFOA/PFOS contamination. *See* Verónica M. Vieira et al., *Perfluorooctanoic Acid Exposure and Cancer Outcomes in a Contaminated Community: A Geographic Analysis*, 121 Env. Health Perspectives 318–23 (Mar. 2013) (showing an overall adjusted odds ratio of 1.1 for multiple myeloma when adjusted for other risk factors).

The absence of alternative risk factors, in combination with medical literature showing increased risk for multiple myeloma based on exposure to PFOA, shows that the Veteran’s current multiple myeloma disability is at least as likely as not caused by exposures in service.

# Skin

## Skin Cancer

#### Agent Orange Associated with Non-Melanoma Skin Cancer

A retrospective review of medical records of patients who enrolled in VA’s Agent Orange registry revealed that “2,3,7,8-Tetrachlorodibenzodioxin exposure appears to be associated with the development of nonmelanotic invasive skin cancer.” Mark W. Clemens *et al.*, *Association Between Agent Orange Exposure and Nonmelanotic Invasive Skin Cancer: A Pilot Study*, 133 Plast. Reconstr. Surg. 432 (2014), available at <https://pubmed.ncbi.nlm.nih.gov/‌24469173/> (abstract enclosed).

# Endocrine

## Diabetes Mellitus

#### Alcohol Use Aggravates Diabetes

* + New medical journal abstract, N.V. Emanuele et al., *Consequences of Alcohol Use in Diabetics*, 22 Alc. Health Res. World 211 (1998), is relevant to show that alcohol use aggravates diabetes.

#### COPD Causes DM

During a 10-year longitudinal cohort study of patients with diagnosed COPD, 19 percent developed DM. Te-Wei Ho et al., *Diabetes Mellitus in Patients with Chronic Obstructive Pulmonary Disease-The Impact on Mortality*, 12 PLoS ONE (2017), available at https://www.‌ncbi.‌nlm.nih.gov/pmc/articles/PMC5391945/pdf/pone.0175794.pdf. Development of DM was most likely among patients with comorbid hypertension, cerebrovascular disease, and coronary artery disease. *Id.* The researchers noted that other “evidence also supports that COPD constitutes an important risk factor for developing incident DM.” *Id.* And “recent reviews have concluded that COPD alone can be considered to be a risk factor for development of DM, as supported by several nationwide and international epidemiological studies. *Id.* (citing Roglian P et al., *Chronic Obstructive Pulmonary Disease and Diabetes*, COPD Research & Practice (2015); Glaser S et al., *Chronic Obstructive Pulmonary Disease and Diabetes Mellitus: A Systematic Review of the Literature*, 89 Respiration 253 (2015)).

#### Lead Exposure Causes Diabetes

* Nexus to lead exposure:
  + New medical literature, Todd Leff *et al.*, *Diabetes and Exposure to Environmental Lead (Pb)*, 6 Toxics 54 (2018), is relevant to show that “demonstrate that lead has deleterious effects on physiological systems that are crucial for the maintenance of normal metabolic balance.”

#### Obesity Causes Diabetes

“The rising incidence of type 2 diabetes among children and adults is related to the epidemic of obesity.” Abdullah S Al-Goblan et al., *Mechanism Linking Diabetes Mellitus and Obesity*, 7 Diabetes, Metabolic Syndrome & Obesity: Targets & Therapy 587, 588 (2014) (enclosed). In fact, “[o]besity is considered the most important factor in the development of metabolic diseases.” *Id.* at 589. The mechanisms of this connection have been well-studied and supported by medical literature; “[i]n an obese individual, the amount of NEFA, glycerol, hormones, cytokines, proinflammatory substances, and other substances that are involved in the development of insulin resistance are increased.” *Id.* at 590.

* + New medical article, Abdullah S Al-Goblan et al., *Mechanism Linking Diabetes Mellitus and Obesity*, 7 Diabetes, Metabolic Syndrome & Obesity: Targets & Therapy 587 (2014), is relevant to show that “[o]besity is considered the most important factor in the development of metabolic diseases.”

## Dyslipidemia

#### PFAS Causes Dyslipidemia

*Guidance on PFAS Exposure, Testing, and Clinical Follow-Up 2022*, Nat’l Acads. Scis. Comm. on Guidance on PFAS Testing & Health Outcomes (2022), available at <https://nap.naptionalacademies.org/26156> (enclosed).

# Neurological Conditions and Convulsive Disorders

## Glioblastoma Brian Cancer

#### Agent Orange Causes Glioblastoma

* Non-presumptive nexus to herbicide-agent exposure:
  + Although the TERA Exception memo indicates that 38 USC 1168(a) does not apply to brain cancers based on NAS research from 1993—more than three decades ago—the general rules of the duty to assist apply and a standard direct service connection medical opinion must be obtained if the claimant shows (1) competent evidence of a current disability or persistent or recurrent symptoms of a disability, and (2) evidence establishing that an event, injury, or disease occurred in service or establishing certain diseases manifesting during an applicable presumptive period for which the claimant qualifies, and (3) an indication that the disability or persistent or recurrent symptoms of a disability may be associated with the veteran’s service or with another service-connected disability, but (4) lacks sufficient competent medical evidence on file for VA to make a decision on the claim.  
      
    Thus, with the nexus support below, a direct service connection medical-opinion is required even though a TERA opinion would not be otherwise necessary.
  + New medical literature Hyun Ah Lee *et al.*, *Long-Term Effects of Defoliant Exposure on Brain Atrophy Progression in Humans*, 92 NeuroTox. 25 (2022), is relevant to show that neurotoxicity from dioxin can damage the brain even 40 years after exposure.
  + New medical literature summary, *Dioxin-Like Chemical Messenger Makes Brain Tumors More Aggressive*, is relevant to show that kynurenin worsens brain tumors and that it has similar pathophysiology to dioxin impacts because it activates dioxin receptor proteins.

## Headaches (Non-Migraine)

#### Anxiety Causes Headaches

Veteran is service connected for anxiety. Headaches can be a common symptom and sometimes a good indicator of an anxiety disorder. And chronic co-occurring headaches can make functioning even more difficult for someone with an anxiety disorder.

“Headaches”. [Headaches | Anxiety and Depression Association of America, ADAA](https://adaa.org/understanding-anxiety/related-illnesses/headaches)

#### Obesity Causes Headaches

Recent research suggests that migraine and obesity may be directly linked. Obesity is related to higher frequency and severity of headache attacks. There is also some evidence to suggest that obesity is associated with migraine prevalence.

“Migraine and Obesity”. [Migraine and Obesity: Epidemiology, Possible Mechanisms, and the Potential Role of Weight Loss Treatment (nih.gov)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2974024/#:~:text=Recent%20research%20suggests%20that%20migraine,among%20individuals%20who%20have%20migraine.&text=There%20is%20also%20some%20evidence,is%20associated%20with%20migraine%20prevalence.)

#### Posttraumatic Stress Disorder (PTSD) Causes Headaches

Medical research shows a significant relationship between PTSD and headaches. In 2009 researchers published the results of an observational, cross-sectional study based on questionnaires completed by 308 veterans of Operation Iraqi Freedom and Operation Enduring Freedom. Niloofar Afari et al., *PTSD, Combat Injury, and Headache in Veterans Returning from Iraq/Afghanistan*, Headache 1267 (2009) (enclosed). Of participating veterans who reported tension or migraine headaches, a significantly larger portion had PTSD than those who did not report headaches—and in turn, PTSD was a significant independent predictor of headaches. *Id.* at 1271–72. The researchers posited several explanations for the mechanisms underlying the relationship between PTSD and headaches. In particular, they noted “evidence that psychological stress is a central contributor to primary headache due to chronic activation of the hypothalamicpituitary-adrenal axis and other physiological systems of the stress response.” *Id.* at 1273. On the other hand, there was evidence that physical trauma that caused PTSD could be associated with headaches, or that PTSD and headaches might have shared underlying genetic factors. *Id.*

Given the medical evidence showing that PTSD is a significant and independent predictor of tension headaches, the evidence is at least in relative equipoise as to whether the Veteran’s tension headache disability is secondary to service-connected PTSD. Service connection must therefore be awarded.

* Nexus to service-connected PTSD:
  + New medical literature, Niloofar Afari et al., *PTSD, Combat Injury, and Headache in Veterans Returning from Iraq/Afghanistan*, Headache 1267 (2009), is relevant to show that veterans who reported tension or migraine headaches, a significantly larger portion had PTSD than those who did not report headaches—and in turn, PTSD was a significant independent predictor of headaches. The researchers posited several explanations for the mechanisms underlying the relationship between PTSD and headaches. In particular, they noted “evidence that psychological stress is a central contributor to primary headache due to chronic activation of the hypothalamicpituitary-adrenal axis and other physiological systems of the stress response.”

#### Refractive (Vision) Error Causes Headaches

* + ­New medical literature Samuel Otabor Wajuihian, *Exploring Correlations Between Headaches and Refractive Errors in an Optometry Clinic Sample*, 20 Brit. & Irish Orthoptic J. 1 (2024), is relevant to show that people with refractive errors are much more prone headaches.

#### Tinnitus Causes or Aggravates Headaches

The Veteran is entitled to service connection for headaches because medical research shows a connection between tinnitus and headaches.

A 2015 study of 193 patients with tinnitus and headache found that “fluctuations in symptom and severity of tinnitus and headache were interrelated.” Berthold Langguth et al., *Tinnitus and Headache*, 2015 BioMed Research Int’l Article ID 797416 (2015), at 1, <https://www.hindawi.com/journals/bmri/2015/‌797416/> (enclosed). Although onset of headache often preceded tinnitus, the researchers also stated that tinnitus can trigger headache. *Id.* at 5. Overall, the researchers concluded there is “a significant relationship between tinnitus and headache laterality and a temporal interaction of both disorders in the majority of cases suggest that the cooccurrence of tinnitus and headache is not purely coincidental but that both disorders may be linked by shared pathophysiological mechanisms.” *Id.*

The medical research thus indicates a causal connection between tinnitus and headaches may, and in fact likely, exists. Resolving reasonable doubt in the Veteran’s favor, therefore, secondary service connection is warranted.

* Nexus to service-connected tinnitus:
  + New medical literature, Berthold Langguth et al., *Tinnitus and Headache*, 2015 BioMed Research Int’l Article ID 797416 (2015), available at <https://www.hindawi.com/journals/bmri/2015/‌797416/>, is relevant to show that there is “a significant relationship between tinnitus and headache laterality and a temporal interaction of both disorders in the majority of cases suggest that the cooccurrence of tinnitus and headache is not purely coincidental but that both disorders may be linked by shared pathophysiological mechanisms.”

## Tinnitus

#### Onset of Tinnitus with Normal Audiogram

In the alternative, medical research in VA’s constructive possession and also enclosed here shows that delayed-onset tinnitus is common. Research funded by VA’s own National Center for Rehabilitative Auditory Research and published in VA’s Progressive Tinnitus Management handbook has shown that 55 percent of adults with tinnitus described a gradual onset—versus just 24 percent with sudden onset and 21 percent who did not know. Jim Henry et al., Progressive Tinnitus Management: Clinical Handbook for Audiologists 5. “Uncertainty about the onset of tinnitus can make it difficult to identify a precipitating event.” *Id.* Further, “*[d]elayed-onset tinnitus* is thought to occur weeks, months, or even years following some precipitating event . . . Evaluating a claim of delayed-onset tinnitus requires taking a detailed history that covers all possible circumstances that might have caused damage to the auditory system.” In addition, a 2016 medical study found that noise exposure can cause tinnitus even without the presence of abnormal puretone thresholds. Hannah Guest et al. *Tinnitus with a Normal Audiogram: Relation to Noise Exposure But No Evidence for Cochlear Synaptopathy*,344 Hearing Research 265 (2017); *see also Noise-Induced Tinnitus*, Audiological Consultants of Atlanta, available at <https://audioconsult.com/services/specialized-testing/noise-induced-tinnitus/> (last visited Aug. 31, 2021) (tinnitus “may or may not occur simultaneously with hearing loss”). The VA-funded research on tinnitus concludes that is seems “likely that noise exposure . . . can result in delayed-onset tinnitus, even when the tinnitus onset occurs years after the event.” Henry, *supra* at 6. This is supported by additional research in the field. *E.g.* Byung In Han et al., *Tinnitus: Characteristics, Causes, Mechanisms, and Treatments*, 5 J. Clin. Neurol. 11–19, 12 (2009) (“In some cases, tinnitus has a gradual onset and several years can pass before an intermittent, low-intensity tinnitus becomes bothersome.”); Audiological Consultants, *supra* (“intermittent pattern often continues for months or years with the periods of tinnitus becoming longer and longer.”).

Thus, the scientific research on tinnitus shows that the Veteran’s current tinnitus disability is plausibly related to the in-service noise exposure. Here, the AOJ erred by relying on a medical opinion that discounted the notion that the Veteran’s tinnitus could be related to service based on a premise ***soundly rejected by VA’s own research***. Further, the opining clinician failed to adequately address any other possible causes of the Veteran’s current tinnitus. Had the clinician done so—as prescribed by VA clinical guidelines set forth above—it would have been obvious that the Veteran has no other possible noise exposures or events that could have caused tinnitus.

In sum, the evidence of record shows a current tinnitus disability and in-service noise exposure. And both the Veteran’s competent lay statements and VA’s own medical literature support a nexus. Service connection for tinnitus is therefore established in this case.

#### Tinnitus Delayed-Onset RO language

* Nexus:
  + New medical treatise, Jim Henry et al., Progressive Tinnitus Management: Clinical Handbook for Audiologists, is relevant to show that 55 percent of adults with tinnitus described a gradual onset—versus just 24 percent with sudden onset and 21 percent who did not know. Further, “*[d]elayed-onset tinnitus* is thought to occur weeks, months, or even years following some precipitating event . . . Evaluating a claim of delayed-onset tinnitus requires taking a detailed history that covers all possible circumstances that might have caused damage to the auditory system.”
  + New medical article, Hannah Guest et al. *Tinnitus with a Normal Audiogram: Relation to Noise Exposure But No Evidence for Cochlear Synaptopathy*,344 Hearing Research 265 (2017), is relevant to show that noise exposure can cause tinnitus even without the presence of abnormal puretone thresholds.
  + New medical article, Byung In Han et al., *Tinnitus: Characteristics, Causes, Mechanisms, and Treatments*, 5 J. Clin. Neurol. 11–19, 12 (2009), is relevant to show that “[i]n some cases, tinnitus has a gradual onset and several years can pass before an intermittent, low-intensity tinnitus becomes bothersome.”

#### Onset of Tinnitus

Medical research in VA’s constructive possession and also enclosed here shows that delayed-onset tinnitus is common. Research funded by VA’s own National Center for Rehabilitative Auditory Research and published in VA’s Progressive Tinnitus Management handbook has shown that 55 percent of adults with tinnitus described a gradual onset—versus just 24 percent with sudden onset and 21 percent who did not know. Jim Henry et al., Progressive Tinnitus Management: Clinical Handbook for Audiologists 5. “Uncertainty about the onset of tinnitus can make it difficult to identify a precipitating event.” *Id.* Further, “*[d]elayed-onset tinnitus* is thought to occur weeks, months, or even years following some precipitating event . . . Evaluating a claim of delayed-onset tinnitus requires taking a detailed history that covers all possible circumstances that might have caused damage to the auditory system.” In addition, a 2016 medical study found that noise exposure can cause tinnitus even without the presence of abnormal puretone thresholds. Hannah Guest et al. *Tinnitus with a Normal Audiogram: Relation to Noise Exposure But No Evidence for Cochlear Synaptopathy*, 344 Hearing Research 265 (2017); *see also Noise-Induced Tinnitus*, Audiological Consultants of Atlanta, available at https://audioconsult.com/services/specialized-testing/noise-induced-tinnitus/ (last visited Aug. 31, 2021) (tinnitus “may or may not occur simultaneously with hearing loss). The VA-funded research on tinnitus concludes that is seems “likely that noise exposure . . . can result in delayed-onset tinnitus, even when the tinnitus onset occurs years after the event.” Henry, *supra* at 6. This is supported by additional research in the field. *E.g.* Byung In Han et al., *Tinnitus: Characteristics, Causes, Mechanisms, and Treatments*, 5 J. Clin. Neurol. 11–19, 12 (2009) (“In some cases, tinnitus has a gradual onset and several years can pass before an intermittent, low-intensity tinnitus becomes bothersome.”); Audiological Consultants, *supra* (“intermittent pattern often continues for months or years with the periods of tinnitus becoming longer and longer.”).

## Migraine

#### Cervical Spine Disability Causes Migraine

Cervicogenic headaches have been a recognized clinical reality since 1983, and “neck pain has become more commonly recognized in migraine, and it may be a predictor of migraine disability.” Naoki Aoyama, *Involvement of Cervical Disability in Migraine: A Literature Review*, 15 Brit. J. of Pain 199, 199 (2020), available at <https://‌www.ncbi.nlm.nih.gov/‌‌pmc/‌articles/‌PMC8138615> (enclosed). Research has shown that patients with neck pain have a “7.6-fold higher risk of developing” chronic migraine disability. *Id.* (citations omitted). “Importantly, 31.3–70% of the patients” studied who had both neck pain and migraines, “developed neck pain before the onset of migraine, suggesting that neck pain may act as a trigger of migraine.” *Id.* at 206.

* Nexus to service-connected neck disability:
  + New medical article Naoki Aoyama, *Involvement of Cervical Disability in Migraine: A Literature Review*, 15 Brit. J. of Pain 199, 199 (2020), available at <https://‌www.ncbi.nlm.nih.gov/‌‌pmc/‌articles/‌PMC8138615>, is relevant to show “that neck pain may act as a trigger of migraine.”

#### Ischemic Heart Disease Associated with Migraine

* + New medical literature, Aisha Saeed et al., *Association of Migraine and Ischemic Heart Disease: A Review*, 11 Cureus e5710 (2019), available at <https://pubmed.ncbi.nlm.nih.gov/31720187/>, is relevant to show that migraines and IHD are strongly associated through multiple potential mechanisms.

#### Mood Disorder Causes Migraine

* Nexus to service-connected psychiatric disorder:
  + New medical literature, K. Rammohan et al., *Migraine and Mood Disorders: Prevalence, Clinical Correlations and Disability*, 10 J. Neurosci. Rural Prac. 28 (2019), available at [https://www.ncbi.nlm.nih.gov/pmc/  
    articles/PMC6337984/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6337984/), is relevant to show that research reveals a plausible bidirectional relationship between migraines and mood disorders, with positive, dose-based correlations between mood symptoms, migraine duration, and sensory symptoms.

#### Obesity Causes Migraine

Obesity is also a recognized cause or aggravator of migraine disability. Dale S. Bnod et al, *Migraine & Obesity: Epidemiology, Possible Mechanisms, & the Potential Role of Weight Loss Treatment*, 12 Obes. Rev. e362 (2011), available at [https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/PMC2974024/](https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/PMC2974024/#:~:text=Recent%20research%20suggests%20that%20migraine,among%20individuals%20who%20have%20migraine.&text=There%20is%20also%20some%20evidence,is%20associated%20with%20migraine%20prevalence) (enclosed). “[o]bese patients [are] 3 times as likely as age-matched normal-weight controls to have migraine.” *Id.* “[T]here is stronger evidence to suggest that obesity exacerbates migraine,” and at least some evidence to show “obesity increases risk for having migraine.” *Id.* Possible mechanisms for the relationship include an “inflammatory state that exists with obesity” that could “exacerbate the inflammatory response in migraine, possibly contributing to headaches that are more frequent or severe.” *Id.* Researchers also posit a connection through adipocytokines which affect metabolism and could also “promote inflammatory processes underlying migraine.” *Id.* Researchers concluded that weight loss might be an effective treatment to alleviate migraine severity. *Id.*

* Nexus through obesity as intermediate step:
  + New medical literature, Dale S. Bond et al, *Migraine & Obesity: Epidemiology, Possible Mechanisms, & the Potential Role of Weight Loss Treatment*, 12 Obes. Rev. e362 (2011), available at [https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/PMC2974024/](https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/PMC2974024/#:~:text=Recent%20research%20suggests%20that%20migraine,among%20individuals%20who%20have%20migraine.&text=There%20is%20also%20some%20evidence,is%20associated%20with%20migraine%20prevalence), is relevant to show that “[o]bese patients [are] 3 times as likely as age-matched normal-weight controls to have migraine.” “[T]here is stronger evidence to suggest that obesity exacerbates migraine,” and at least some evidence to show “obesity increases risk for having migraine.” Possible mechanisms for the relationship include an “inflammatory state that exists with obesity” that could “exacerbate the inflammatory response in migraine, possibly contributing to headaches that are more frequent or severe.” Researchers also posit a connection through adipocytokines which affect metabolism and could also “promote inflammatory processes underlying migraine.”

#### Back Pain Causes Migraine

* Secondary nexus to service-connected chronic back pain:
  + New medical literature abstract, P.N. Duckro et al., *Migraine as a Sequela to Chronic Low Back Pain*, 34 Headache 279 (1994), finds that “headache was found to have begun or exacerbated markedly after onset of low back pain.”

#### Particulate Matter Causes or Aggravates Migraine

“Past research links short-term exposure to a range of air pollutants with ED visits [for] migraine headaches.” Holly Elser et al., *Air Pollution, Methane Super-Emitters, and Oil & Gas Wells in Northern California: The Relationship with Migraine Headache Prevalence & Exacerbation*, 20 Env. Health (2021), <https://ehjournal.biomedcentral.com/‌track/‌pdf/‌10.1186/‌s12940-021-00727-w.pdf> (enclosed). A 2021 case-control study and case-case analysis using data from nearly 1.5 million individuals revealed “increased odds of exposure to NO2 and methane super-emitters among patients with migraine as compared with frequency-matched population controls without clinical diagnosis of migraine. . . . [And] migraine severity–as measured by frequency of triptan prescriptions, outpatient neurology visits, migraine-specific urgent care and ED visits, and MPA score–was most strongly and consistently associated with average PM2.5 and NO2 exposure.” *Id.* Thus, medical research shows that the Veteran’s presumed exposure to particulate matter at least as likely as not caused or aggravated his migraine disability.

* Nexus to particulate-matter exposure:
  + New medical literature, Holly Elser et al., *Air Pollution, Methane Super-Emitters, and Oil & Gas Wells in Northern California: The Relationship with Migraine Headache Prevalence & Exacerbation*, 20 Env. Health (2021), <https://ehjournal.biomedcentral.com/‌track/‌pdf/‌10.1186/‌s12940-021-00727-w.pdf>, is relevant to show that there are “increased odds of exposure to NO2 and methane super-emitters among patients with migraine as compared with frequency-matched population controls without clinical diagnosis of migraine. . . . [And] migraine severity–as measured by frequency of triptan prescriptions, outpatient neurology visits, migraine-specific urgent care and ED visits, and MPA score–was most strongly and consistently associated with average PM2.5 and NO2 exposure.”

#### Posttraumatic Stress Disorder (PTSD) Causes Migraine

“A growing body of epidemiological literature supports an association between migraine and PTSD.” B. Lee Peterlin, et al., *Post-Traumatic Stress Disorder & Migraine: Epidemiology, Sex Differences, & Potential Mechanisms*, 51 Headache 860 (2011) (enclosed). “[O]f those with episodic migraine and PTSD, 69% reported symptoms related to PTSD before the onset of severe or frequent headache.” *Id.* Researchers have therefore posited that mechanisms of association could include autonomic dysfunction, abnormal cortisol levels, and immune abnormatlities; “it is possible that having PTSD which is associated with low cortisol levels, results in an increase in proinflammatory cytokines and contributes to migraine development or maintenance.” *Id.* In conclusion, researchers put forth that “[t]he presence of PTSD in migraineurs is associated with greater headache-related disability than in migraineurs without PTSD; . . . and data suggest that behavioral PTSD treatment alone can positively influence chronic pain conditions and disability.” *Id.* (footnotes omitted).

* Nexus to service-connected PTSD:
  + New medical literature, B. Lee Peterlin, et al., *Post-Traumatic Stress Disorder & Migraine: Epidemiology, Sex Differences, & Potential Mechanisms*, 51 Headache 860 (2011), is relevant to show that “[O]f those with episodic migraine and PTSD, 69% reported symptoms related to PTSD before the onset of severe or frequent headache.” Researchers have therefore posited that mechanisms of association could include autonomic dysfunction, abnormal cortisol levels, and immune abnormatlities; “it is possible that having PTSD which is associated with low cortisol levels, results in an increase in proinflammatory cytokines and contributes to migraine development or maintenance.” In conclusion, researchers put forth that “[t]he presence of PTSD in migraineurs is associated with greater headache-related disability than in migraineurs without PTSD; . . . and data suggest that behavioral PTSD treatment alone can positively influence chronic pain conditions and disability.”

#### Tinnitus Causes Migraine

The Veteran is entitled to service connection for migraine headaches because medical research shows a connection between tinnitus and headaches.

A 2015 study of 193 patients with tinnitus and headache found that 44.6 percent of the patients suffered from migraines and “fluctuations in symptom and severity of tinnitus and headache were interrelated.” Berthold Langguth et al., *Tinnitus and Headache*, 2015 BioMed Research Int’l Article ID 797416 (2015), at 1, available at <https://www.hindawi.com/journals/bmri/2015/‌797416/> (enclosed). Although onset of headache often preceded tinnitus, the researchers also stated that tinnitus can trigger headache. *Id.* at 5. Overall, the researchers concluded there is “a significant relationship between tinnitus and headache laterality and a temporal interaction of both disorders in the majority of cases suggest that the cooccurrence of tinnitus and headache is not purely conincidental but that both disorders may be linked by shared pathophysiological mechanisms.” *Id.*

The medical research thus indicates a causal connection between tinnitus and migraine headaches may, and in fact likely, exists. Resolving reasonable doubt in the Veteran’s favor, therefore, secondary service connection is warranted.

* Nexus to service-connected tinnitus:
* New medical literature, Berthold Langguth et al., *Tinnitus and Headache*, 2015 BioMed Research Int’l Article ID 797416 (2015), available at <https://www.hindawi.com/journals/bmri/2015/‌797416/>, is relevant to show that there is “a significant relationship between tinnitus and headache laterality and a temporal interaction of both disorders in the majority of cases suggest that the cooccurrence of tinnitus and headache is not purely conincidental but that both disorders may be linked by shared pathophysiological mechanisms.”

## Peripheral Neuropathy

#### Agent Orange Causes Late Onset PN

The availability of presumptive service connection for some conditions for veterans does not preclude the applicability of other theories of entitlement—to include direct service connection. *Stefl v. Nicholson*, 21 Vet. App. 120, 123 (2007) (reasoning availability of presumptions for herbicide agents does not preclude direct service connection). Enclosed is a medical treatise article showing significant causal likelihood between Vietnam War era exposure and peripheral neuropathy (PN) clinically diagnosed 25 to 30 years after exposure.

* Non-presumptive nexus to herbicide-agent exposure:
  + Although the TERA Exception memo indicates that 38 USC 1168(a) does not apply to chronic peripheral nervous system disorders (other than early-onset peripheral neuropathy) based on NAS research from 1993—more than three decades ago—the general rules of the duty to assist apply and a standard direct service connection medical opinion must be obtained if the claimant shows (1) competent evidence of a current disability or persistent or recurrent symptoms of a disability, and (2) evidence establishing that an event, injury, or disease occurred in service or establishing certain diseases manifesting during an applicable presumptive period for which the claimant qualifies, and (3) an indication that the disability or persistent or recurrent symptoms of a disability may be associated with the veteran’s service or with another service-connected disability, but (4) lacks sufficient competent medical evidence on file for VA to make a decision on the claim.  
      
    Thus, with the nexus support below, a direct service connection medical-opinion is required even though a TERA opinion would not be otherwise necessary.
  + New medical literature, Suzanne M. de la Monte and Anuva Goel, *Agent Orange Reviewed: Potential Role in Peripheral Neuropathy and Neurodegeneration*, ZK30 J. Mil. Vets. Health 17 (2022), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9920643/> (enclosed), is relevant to show a significant causal likelihood between Vietnam War era exposure and peripheral neuropathy clinically diagnosed 25 to 30 years after exposure.

# Mental Disorders

## Depression

#### GERD Causes Depression

In 2018, researchers conducted two nested case-control studies, one comparing nearly 61,000 participants with depression to more than 240,000 control participants, and a second study comparing over 133,000 participants with GERD to more than 266,000 participants without. So Young Kim et al., *Bidirectional Association Between Gastroesophageal Reflux Disease and Depression: Two Different Nested Case-Control Studies Using a National Sample Cohort*, 8:11748 Nature Scientific Reps. at 1 (2018) https://www.nature.com/articles/s41598-018-29629-7.pdf. The rate of GERD in the depression group was 16.3 percent compared with 9 percent in the control, and the rate of depression in the GERD group was 5.7 percent versus 3.9 percent in the control. *Id.* at 2. The results were consistent across all age and gender groups. *Id.*

The researchers offered multiple well-reasoned explanations for this association—including theories that GERD may cause or aggravate depression:

We have identified several possible explanations for the observation that GERD increased the risk of depression. First, the esophageal mucosa of patients with GERD contains large amounts of cytokines, such as interleukin (IL)-6, IL-8, IL-1beta, interferon gamma (IFN-γ), and tumor necrosis factor alpha (TNF-α)[]. The increased levels of these immune mediators in peripheral organs might be associated with the upregulation of central nervous system inflammation[], which might affect depression and bipolar disorder[]. Second, frequent arousal by GERD might activate the autonomic nervous system and increase sympathetic activation[]. Acid reflux stimulates the vagus nerve and triggers bronchoconstriction21, which could result in sleep disorders and affect mood disorders[]. Third, the reflux symptom itself could result in depression if patients are constantly feeling upset about their condition[].

*Id.* (footnotes omitted).

These concerns were echoed in a 2019 cross-sectional study of 258 patients with GERD, among whom 41.4 percent had depression, 34.4 percent had anxiety, and 27.13 percent had both. Saleh Mohammed Channa, *Depression and Anxiety in Patients with and Without Chest Pain*, 11(11) Cureus e6103, 1 (Nov. 8, 2019) https://www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC6858267/pdf/cureus-0011-00000006103.pdf. The researchers explained that “GERD imposes negative effects on [quality of life], which can both exacerbate and be exacerbated by depression and anxiety.” *Id.* at 4.

Given the statistical increase in risk for depression among GERD patients, and the equally plausible theories that GERD causes or aggravates depression, the evidence of record is at least in relative equipoise and the Veteran is entitled to service connection for depression on a secondary basis.

#### Obstructive sleep apnea (OSA) Aggravates Depression

[For Individuals with Obstructive Sleep Apnea, Institution of CPAP therapy is Associated with an Amelioration of Symptoms of Depression which is Sustained Long Term | Journal of Clinical Sleep Medicine (aasm.org)](https://jcsm.aasm.org/doi/10.5664/jcsm.26975)

#### Pain Causes Depression

“Clinical studies have revealed that chronic pain, as a stress state, often induced depression . . . and that up to 85% of patients with chronic pain are affected by severe depression.” Jiyao Sheng et al., *The Link Between Depression and Chronic Pain: Neural Mechanisms in the Brain*, 2017 Neural Plasticity 1, available at <https://‌www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC5494581/> (2017) (enclosed). Pain and depression are linked both in initial occurrence and progression. *Id.* Chronic pain and depression are linked through multiple mechanisms; not only is there the basic logical connection between chronically experiencing pain and feeling down or worse about life, but there “may be . . . common neuroplasticity mechanism changes, which are a potentially important route for the onset and aggravation of chronic pain and depression.” *Id.* at 2.

* Nexus to service-connected painful disabilities:
  + New medical literature, Jiyao Sheng et al., *The Link Between Depression and Chronic Pain: Neural Mechanisms in the Brain*, 2017 Neural Plasticity 1, available at <https://‌www.ncbi.nlm.nih.gov/‌pmc/‌articles/‌PMC5494581/> (2017), is relevant to show that “Clinical studies have revealed that chronic pain, as a stress state, often induced depression . . . and that up to 85% of patients with chronic pain are affected by severe depression.” Pain and depression are linked both in initial occurrence and progression. Chronic pain and depression are linked through multiple mechanisms; not only is there the basic logical connection between chronically experiencing pain and feeling down or worse about life, but there “may be . . . common neuroplasticity mechanism changes, which are a potentially important route for the onset and aggravation of chronic pain and depression.”

#### Tinnitus Causes Depression, Anxiety, Stress

* Nexus to service-connected tinnitus:
  + New medical literature, Jay M. Bhatt *et al.*, *Relationships Between Tinnitus and the Prevalence of Anxiety and Depression*, 127 Laryngoscope 466 (2016), available at <https://pmc.ncbi.nlm.nih.gov/articles/PMC5812676/>, is relevant to show that “[f]or those reporting and seeking treatment of bothersome and intolerable tinnitus, however, it has been suggested that the tinnitus precept may produce an inappropriate activation of the limbic and sympathetic components of the autonomic nervous systems.. . . The consequent hyperactive state can be concomitant with and can contribute to anxiety, depression, and panic and sleep disorder symptoms.”

## Mood Disorder

#### Migraine Causes Mood Disorder

* Nexus to service-connected migraines:
  + New medical literature, K. Rammohan et al., *Migraine and Mood Disorders: Prevalence, Clinical Correlations and Disability*, 10 J. Neurosci. Rural Prac. 28 (2019), available at [https://www.ncbi.nlm.nih.gov/pmc/  
    articles/PMC6337984/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6337984/), is relevant to show that research reveals a plausible bidirectional relationship between migraines and mood disorders, with positive, dose-based correlations between mood symptoms, migraine duration, and sensory symptoms.

#### Alcohol Use as Self-Medication of Mood Disorders

* + New medical literature, James M. Bolton et al., *Self-Medication of Mood Disorders with Alcohol and Drugs in the National Epidemiological Survey on Alcohol and Related Conditions*, 115 J. Affect Disords. 367 (2008), is relevant to show that the veteran’s substance or alcohol use is at least as likely as not a result of a mood disorder and not the other way around.

# Dental and Oral Conditions

# Causes of Obesity

#### Diabetes Causes Obesity

#### Physical and mental disabilities cause obesity

* Nexus to service-connected disabilities through obesity:
  + New article Tsan-Hon Liou *et al.*, *Physical Disability and Obesity*, 63 Nutr. Rev. 321 (2005), available at <https://pubmed.ncbi.nlm.nih.gov/16295145/>, is relevant to show that “people with physical disabilities have a 1.2- to 3.9-fold increase in obesity prevalence” perhaps due to “pathophysiological changes of body composition and energy metabolism, physical inactivity, and muscle atrophy all favor the development of obesity.”
  + New article Francesco Weiss *et al.*, *Psychiatric Aspects of Obesity: A Narrative Review of Pathophysiology and Psychopathology*, 9 J. Clin. Med. 2344 (2020), available at <https://www.mdpi.com/2077-0383/9/8/2344/htm>, is relevant to show that “[e]xecutive dysfunctions” commonly associated with mood disorders “such as poor inhibitory control and increased delay discounting rate, could lead to detrimental eating patterns, whether in quantitative terms . . . or in qualitative terms . . . and disincline the subject to undertake lasting effective changes in diet and lifestyle.”

#### Obesity Opinion Must Address More than Just Calories In vs. Calories Out

The AOJ erred by rejecting the theory of causation or aggravation through obesity based on an inadequate medical opinion. The clinician stated that obesity and weight gain are the result of calorie surplus, and the AOJ relied on this opinion without addressing the Veteran’s contentions.

As an initial matter, the opinion fails to address the question of etiology. Rather, the clinician explained the pathophysiological mechanisms of obesity. The Veteran does not dispute that the primary driver of weight gain is calories in versus calories out (although current research raises the plausibility of additional mechanisms (*see e.g.*, Adela Hruby and Frank B. Hu, *The Epidemiology of Obesity: A Big Picture*, 33 Pharmacoeconomics 673 (2015), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4859313/> (enclosed))). But that simple fact is not responsive to the question of whether the Veteran’s service-connected primary disability was a substantial factor in the Veteran’s weight gain. In that respect, the Court has determined that obesity is properly seen as an intermediate step in secondary service connection where a physical or mental disability causes the mechanical imbalance of calories. *See Garner*, 33 Vet. App. at 248.

But more than that, the medical opinion shows the clinician did not consider the complexities of the mental and physical disabilities that many Veterans wrestle with, and is not up to date on the current research regarding obesity. Obesity is a complex, multifactorial condition that is the result of the interaction of risk factors not completely understood. *The Epidemiology of Obesity*, *supra*.

Medical studies have shown that “people with physical disabilities have a 1.2- to 3.9-fold increase in obesity prevalence” perhaps due to “pathophysiological changes of body composition and energy metabolism, physical inactivity, and muscle atrophy all favor the development of obesity.” Tsan-Hon Liou *et al.*, *Physical Disability and Obesity*, 63 Nutr. Rev. 321 (2005), available at <https://pubmed.ncbi.nlm.nih.gov/16295145/> (abstract enclosed). And psychiatric disability has what is likely a bidirectional causal relationship “since obesity has been repeatedly associated with manifold neuropsychic dysfunctions and, concurrently, varied subsets of psychiatric patients have consistently been shown to be burdened with an increased risk of developing obesity.” Francesco Weiss *et al.*, *Psychiatric Aspects of Obesity: A Narrative Review of Pathophysiology and Psychopathology*, 9 J. Clin. Med. 2344 (2020), available at <https://www.mdpi.com/2077-0383/9/8/2344/htm> (enclosed). Researchers explain that “[e]xecutive dysfunctions” commonly associated with mood disorders “such as poor inhibitory control and increased delay discounting rate, could lead to detrimental eating patterns, whether in quantitative terms . . . or in qualitative terms . . . and disincline the subject to undertake lasting effective changes in diet and lifestyle.” *Id.*

PTSD in particular—for which the Veteran is service-connected—is a well-recognized cause leading to obesity. Olivia M. Farr et al., *Stress- and PTSD-Associated Obesity and Metabolic Dysfunction: A Growing Problem Requiring Further Research and Novel Treatments*, 63 Metabolism 1463 (2014) (enclosed). The specific mechanisms for this relationship are not known for certain, but several explanations have been proffered in the medical research: “sympathetic nervous system activation and the release of stress hormones by the hypothalamic-pituitary-adrenal axis,” “neural changes known to occur in PTSD that may lead to altered cognitive/central control of feeding behaviors,” altered cognition “leading to altered consumptive behaviors,” “altered control of appetite hormones,” or effects on inflammatory markers. *Id.* “It is clear,” researchers have concluded, “that, regardless of the mechanism, PTSD leads to obesity, which eventually links to significant obesity-related complications.” *Id.*

The clinician’s failure to provide a holistic review of the causes of the Veteran’s obesity, beyond the surface-level mechanisms of unhealthy eating habits or lack of activity, indicates that the examiner is not qualified to provide the medical opinion necessary in this case. Either the examiner has not studied the topic of obesity sufficiently, or the examiner is affected by an anti-obesity bias that is highly prevalent among healthcare providers and has been shown to negatively affect clinicians’ judgment and care. *See* Keith Norris, *Health Care Systems Perspectives, in* Addressing Structural Racism, Bias, and Health Communication as Foundational Drivers of Obesity 30–32 (proceedings of a 2021 workshop series) (enclosed). *See also* Kimberly Gudzune, *The Effect of Obesity on Patient–Provider Communication, in* Drivers of Obesity *supra*, 126–129 (enclosed).

#### PTSD Causes Obesity

The Court has noted that the theory of secondary service connection through obesity as an intermediate step may be reasonably raised in cases involving:

mobility limitations or reduced physical activity as a result of a service-connected physical disability . . . ; reduced physical activity or inability to follow a course of exercise or diet as a result of service-connected mental disability; side effects of medication . . . ; treatise evidence suggesting a connection between all or some combination of obesity, service-connected disability, and the claimed condition; lay statements by a veteran attributing weight gain or obesity to the service-connected disability; and statements by treating physicians or medical examiners attributing weight gain or obesity to the service-connected disability.

*Garner*, 33 Vet. App. at 248 (footnotes omitted). The Court noted that this list is not exclusive. *Id.* at 249.

As the Court itself has stated, and as the medical research establishes, the prevalence of obesity among patients with PTSD is not simply a choice. Rather, it may be linked to several physiological causes or to a veteran’s “inability to follow a course of exercise or diet as a result of service-connected mental disability” or another factor. *See id.* at 248.

PTSD is a well-recognized cause leading to obesity. Olivia M. Farr et al., *Stress- and PTSD-Associated Obesity and Metabolic Dysfunction: A Growing Problem Requiring Further Research and Novel Treatments*, 63 Metabolism 1463 (2014) (enclosed). The specific mechanisms for this relationship are not known for certain, but several explanations have been proffered in the medical research: “sympathetic nervous system activation and the release of stress hormones by the hypothalamic-pituitary-adrenal axis,” “neural changes known to occur in PTSD that may lead to altered cognitive/central control of feeding behaviors,” altered cognition “leading to altered consumptive behaviors,” “altered control of appetite hormones,” or effects on inflammatory markers. *Id.* “It is clear,” researchers have concluded, “that, regardless of the mechanism, PTSD leads to obesity, which eventually links to significant obesity-related complications.” *Id.*

Those complications include disability. [insert evidence linking obesity to disability claimed].

* + New medical article, Olivia M. Farr et al., *Stress- and PTSD-Associated Obesity and Metabolic Dysfunction: A Growing Problem Requiring Further Research and Novel Treatments*, 63 Metabolism 1463 (2014), is relevant to show that PTSD is a well-recognized cause leading to obesity, including through possible mechanisms of “sympathetic nervous system activation and the release of stress hormones by the hypothalamic-pituitary-adrenal axis,” “neural changes known to occur in PTSD that may lead to altered cognitive/central control of feeding behaviors,” altered cognition “leading to altered consumptive behaviors,” “altered control of appetite hormones,” or effects on inflammatory markers. “It is clear,” researchers have concluded, “that, regardless of the mechanism, PTSD leads to obesity, which eventually links to significant obesity-related complications.”

# Miscellaneous Exposure Issues

## Persian Gulf Presumption Language for RO

* This Persian Gulf 1117 and 1119 Veteran is entitled to presumptive service connection for this disability if any one of the following is true:
  + The disability is undiagnosed; or
  + The disability is diagnosed, but the etiology of the Veteran’s specific case is unexplained; or
  + The disability is diagnosed, but the pathophysiology of the Veteran’s specific case is unexplained.

## PFOA / PFAS Exposure Sites

Perfluorooctane sulfonate (PFAS) has been the subject of rising health concerns over the past decades. The “forever chemicals,” as they’re called by environmental groups, are a component of aqueous film-forming foam, which is used in firefighting by the military. Jared Hayes and Scott Faber, *For Decades, the Department of Defense Knew Firefighting Foams With ‘Forever Chemicals’ Were Dangerous But Continued Their Use*, EWG, <https://www.ewg.org/research/decades-department-defense-knew-firefighting-foams-forever-chemicals-were-dangerous> (Mar. 6, 2020). As early as 1973, the U.S. Air Force recognized that firefighting foam was toxic. Ronald H. Kroop and Joseph E. Martin, *Treatability of Aqueous Film-Forming Foams Used for Fire Fighting*, Tech. Rep. No. AFWL-TR-73-279 (Feb. 1974) (enclosed). In the years that followed, the Navy and Army made similar recognitions of the toxicity of firefighting foam and PFAS.

The National Defense Authorization Act for Fiscal Year 2020 mandated that DoD phase out use of PFAS-containing firefighting foam by 2024. But clean-up of contaminated sites could take decades.

PFAS makes its way into ground and drinking water and EPA has issued iterative health advisories for PFAS, reducing the recommended exposure limits each time. Currently, EPA has issued a health advisory recommending exposures through drinking water no greater than 0.02 parts per trillion (ppt). *Drinking Water Health Advisories for PFAS Fact Sheet for Communities*, EPA (enclosed).

Environmental research by DoD and the Environmental Working Group has revealed the presence of PFAS above recommended exposure levels at xxx. Water testing showed the presence of these toxic chemicals at a concentration of xxx—much higher than the EPA-recommended limit of 0.02 ppt.

## Camp Lejeune

#### ASTDR Study Underestimates Odds Ratio

The clinician’s factual basis for the risk of prostate cancer due to exposure at Camp Lejeune is not accurate. The study by the Agency for Toxic Substances and Disease Registry (ASTDR), on which the clinician relied, is fundamentally flawed because the data compared risk of disabilities among marines who served at Lejeune with marines who served at Camp Pendleton. ASTDR chose marines who served at Camp Pendleton based on the premise that they were “similar unexposed cohorts.” *ATSDR Assessment of the Evidence for the Drinking Water Contaminants at Camp Lejeune and Specific Cancers and Other Diseases*, CDC ATSDR (Jan. 13, 2017), available at <https://www.atsdr.cdc.gov/sites/lejeune/Assessment-of-Evidence.html> (enclosed).

But the U.S. Environmental Protection Agency identified Camp Pendleton as a superfund cleanup site, noting TCE and other contaminants in the groundwater and soil. *Superfund Site: Camp Pendleton Marine Corps Base*, EPA, <https://cumulis.epa.gov/supercpad/‌SiteProfiles/‌‌index.cfm?‌fuseaction‌=second‌‌.Cleanup&id‌=0902732> (last visited Oct. 24, 2022) (enclosed). Therefore, Camp Pendleton may have a higher-than-average incidence of disabilities such as prostate cancer due to the presence of toxic contaminants similar to those found at Camp Lejeune. As a result, ASTDR’s comparison study juxtaposes data not from a group exposed to contaminants and a group with no exposure, but rather two groups with exposures. Therefore, Camp Pendleton was not an appropriate choice for control group to assess the odds ratio of prostate cancer incidence or mortality among exposed servicemembers versus the general population. As a result of this poor choice of control group, the ASTDR report likely underestimates the true odds ratio that would represent the increased risk factor for the Veteran’s prostate cancer due to his exposure at Camp Lejeune.