

## GULF WAR ILLNESS

No Updates this Week for Gulf War Illness or Chronic Multisymptom Illness.

## CHRONIC FATIGUE SYNDROME

### [Effects of a short-term aquatic exercise intervention on symptoms and exercise capacity in individuals with chronic fatigue syndrome/myalgic encephalomyelitis: a pilot study.](#)

[Broadbent S<sup>1</sup>](#), [Coetzee S<sup>2</sup>](#), [Beavers R<sup>2</sup>](#).

Eur J Appl Physiol. **2018 Jun 19**. doi: 10.1007/s00421-018-3913-0. PMID: 29923110. [Epub ahead of print]

**PURPOSE:** This pilot pre-and post-intervention study investigated the effects of a short-term aquatic exercise programme on physiological outcomes, symptoms and exercise capacity in women with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME).

**METHODS:** Eleven women (54.8 ± 12.4 year) volunteered for the 5-week program; an initial 20-min aquatic exercise session then two self-paced 20-min sessions per week for 4 weeks. Pre- and post-intervention outcomes were physiological measures, 6 min Walk Test (6MWT), perceived exertion (RPE), hand grip strength, Sit-to-Stand, Sit-Reach test, Apley's shoulder test, FACIT questionnaire, and 24-h post-test tiredness and pain scores (0-10 visual analogue scale). Heart rates, RPE, 24- and 48-h post-session tiredness/pain scores were recorded each session.

**RESULTS:** 6MWT distance increased by 60.8 m (p = 0.006), left hand grip strength by 6 kg (p = 0.038), Sit-Reach test by 4.0 cm (p = 0.017), right shoulder flexibility by 2.9 cm (p = 0.026), FACIT scores by 8.2 (p = 0.041); 24-h post-test tiredness and pain decreased by 1.5 and 1.6, respectively (p = 0.002). There were significant post-intervention increases in exercising heart rates (6MWT 4- and 6-min time points), oxygen saturation at 2-min, and reduced RPE at 4-min. Weekly resting and exercising heart rates increased significantly during the study but RPE decreased; immediately post- and 24-h post-session tiredness decreased significantly. There were no reports of symptom exacerbation.

**CONCLUSIONS:** Five weeks of low-moderate intensity aquatic exercise significantly improved exercise capacity, RPE and fatigue. This exercise mode exercise may potentially be a manageable and safe physical activity for CFS/ME patients.

### [Myalgic encephalomyelitis/chronic fatigue syndrome and the biopsychosocial model: a review of patient harm and distress in the medical encounter.](#)

[Geraghty KJ<sup>1</sup>](#), [Blease C<sup>2</sup>](#).

Disabil Rehabil. **2018 Jun 21**:1-10. doi: 10.1080/09638288.2018.1481149. PMID: 29929450. [Epub ahead of print]

**OBJECTIVE:** Despite the growing evidence of physiological and cellular abnormalities in myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS), there has been a strong impetus to tackle the illness utilizing a biopsychosocial model. However, many sufferers of this disabling condition report distress and dissatisfaction following medical encounters. This review seeks to account for this discord.

**METHODS:** A narrative review methodology is employed to synthesize the evidence for potential iatrogenesis.

**RESULTS:** We identify seven potential modalities of iatrogenesis or harm reported by patients: difficulties in reaching an acceptable diagnosis; misdiagnosis, including of other medical and psychological conditions; difficulties in accessing the sick role, medical care and social support; high levels of patient dissatisfaction with the quality of medical care; negative responses to controversial therapies (cognitive behavioral therapy and graded exercise therapy); challenges to the patient narrative and experience; psychological harm (individual and collective distress).

**CONCLUSION:** The biopsychosocial framework currently applied to ME/CFS is too narrow in focus and fails to adequately incorporate the patient narrative. Misdiagnosis, conflict, and harm are observable outcomes where doctors' and patients' perspectives remain incongruent. Biopsychosocial practices should be scrutinized for potential harms. Clinicians should consider adopting alternative patient-centred approaches. Implications for rehabilitation Patients with ME/CFS may report or experience one or more of the modalities of harms and distress identified in this review. It is important health and rehabilitation professionals seek to avoid and minimize harms when treating or assisting ME/CFS patients. There are conflicting models of ME/CFS; we highlight two divergent models, a biopsychosocial model and a biomedical model that is preferred by patients. The 'biopsychosocial framework' applied in clinical practice promotes treatments such as cognitive behavioral therapy and exercise therapy, however, the evidence for their success is contested and many patients reject the notion their illness is perpetuated by dysfunctional beliefs, personality traits, or behaviors. Health professionals may avoid conflict and harm causation in ME/CFS by adopting more concordant 'patient-centred' approaches that give greater prominence to the patient narrative and experience of illness.

## HEADACHE and MIGRAINE

**Cluster headache is associated with unhealthy lifestyle and lifestyle-related comorbid diseases: Results from the Danish Cluster Headache Survey.**

[Lund N](#)<sup>1</sup>, [Petersen A](#)<sup>1</sup>, [Snoer A](#)<sup>1</sup>, [Jensen RH](#)<sup>1</sup>, [Barloese M](#)<sup>2</sup>.

Cephalalgia. 2018 Jan 1:333102418784751. doi: 10.1177/0333102418784751. PMID: 29933701. [Epub ahead of print]

**Aim:** To compare the prevalence of unhealthy lifestyle factors and comorbid disorders in cluster headache patients with headache-free controls, in order to discuss pathophysiology and possible consequences.

**Methods:** Cluster headache patients from the Danish cluster headache survey aged 18-65 years, diagnosed according to ICHD-II, were compared to sex- and age-matched headache-free controls. Participants completed questionnaires and structured interviews.

**Results:** A total of 400 cluster headache patients and 200 controls participated. Patients had a more unhealthy lifestyle compared with controls in the form of current and current/former smoking (48.3% vs. 9.0%,  $p < 0.001$  and 74.5% vs. 30.0%,  $p < 0.001$ , respectively), higher average alcohol intake per week (98.2 grams vs. 77.9 grams,  $p = 0.033$ ) and BMI (26.1 vs. 24.2 kg/m<sup>2</sup>,  $p < 0.001$ ), whereas coffee and energy drink consumption was equally distributed. Further, lifestyle-related, psychiatric and pain-related diseases were much more prevalent in patients compared with controls, except for diabetes. Sub-group analyses revealed that current/former smokers had a worse clinical presentation than never smokers.

**Conclusion:** Unhealthy lifestyle factors and lifestyle-related diseases were more prevalent in cluster headache patients compared to controls. As lifestyle-related diseases might have serious consequences in the management of cluster headache, it is key to inform patients at an early time point about the possible risks of their lifestyle choices.

**Gray matter volume modifications in migraine: A cross-sectional and longitudinal study.**

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Neurology. 2018 Jun 20. pii: 10.1212/WNL.0000000000005819. doi: 10.1212/WNL.0000000000005819. PMID: 29925551.

[Epub ahead of print]

**OBJECTIVE:** To explore cross-sectional and longitudinal gray matter (GM) volume changes in patients with migraine and their association with patients' clinical characteristics and disease activity.

**METHODS:** Brain T2-weighted and 3-dimensional T1-weighted scans were acquired from 73 episodic migraineurs and 46 age- and sex-matched nonmigraine controls at baseline. Twenty-four migraineurs and 25 controls agreed to be reexamined after a mean follow-up of 4 years. Using a general linear model and SPM12, a whole-brain analysis was performed to assess GM volume modifications.

**RESULTS:** At baseline, compared to controls, patients with migraine showed lower cerebellar GM volume and higher volume of regions of the frontotemporal lobes. At follow-up, migraineurs were significantly older than controls. Over the follow-up, migraineurs developed an increased volume of frontotemporoparietal regions, which was more prominent in patients with a higher baseline disease activity: long disease duration and high attack frequency. Migraineurs also developed decreased GM volume of visual areas, which was related to higher pain severity. Patients with an increased attack frequency at follow-up experienced both increased and decreased volume of nociceptive regions. In migraineurs, reduced GM volume of extrastriate visual areas during the follow-up was significantly correlated to baseline disease activity: shorter disease duration and lower attack frequency.

**CONCLUSION:** In this cohort, the migraine brain changes dynamically over time, and different pathophysiologic mechanisms can occur in response to patients' disease severity. The interaction between predisposing brain traits and experience-dependent responses might vary across different nociceptive and visual areas, thus leading to distinct patterns of longitudinal GM volume changes.

## HEADACHE and MIGRAINE (Continued)

**Impact of Aura and Status Migrainosus on Readmissions for Vascular Events After Migraine Admission.**

[Velickovic Ostojevic L](#)<sup>1</sup>, [Liang JW](#)<sup>2</sup>, [Sheikh HU](#)<sup>1</sup>, [Dhamoon MS](#)<sup>3</sup>.

Headache. **2018 Jun 22**. doi: 10.1111/head.13347. PMID: 29933509. [Epub ahead of print]

**OBJECTIVE:** To estimate readmission rates for acute ischemic stroke (AIS), transient ischemic attack (TIA), subarachnoid hemorrhage, and intracerebral hemorrhage after an index admission for migraine, using nationally representative data.

**METHODS:** The Nationwide Readmissions Database was designed to analyze readmissions for all payers and uninsured, with data on >14 million US admissions in 2013. We used International Classification of Diseases, Ninth Revision, Clinical Modification codes to identify index migraine admissions with and without aura or status migrainosus, and readmissions for cerebrovascular events. Cox proportional hazards regression was performed for each outcome with aura and status migrainosus as main predictors, adjusting for age and vascular risk factors.

**RESULTS:** Out of 12,448 index admissions for migraine, 9972 (80.1%) were women, mean age was 45.5 ± 14.8 years, aura was present in 3038 (24.41%), and status migrainosus in 1798 (14.44%). The 30-day readmission rate (per 100,000 index admissions) was 154 for ischemic stroke, 86 for TIA, 42 for subarachnoid hemorrhage, and 17 or intracranial hemorrhage. In unadjusted models, aura was significantly associated with TIA (hazard ratio 2.43, 95% CI 1.39-4.24), but not AIS (1.26, 0.73-2.18), intracranial hemorrhage (1.86, 0.45-7.79) or subarachnoid hemorrhage (1.85, 0.44-7.75). When adjusting for age and vascular risk factors, aura remained significantly associated with TIA (2.13, 1.22-3.74). Status, in adjusted models, was significantly associated with subarachnoid hemorrhage readmission (4.83, 1.09-21.42).

**CONCLUSIONS:** In this large, nationally representative retrospective cohort study, migraine admission with aura was independently associated with TIA readmission, and status migrainosus was independently associated with subarachnoid hemorrhage. Further research would clarify the role of misdiagnosis and causal relationships underlying these strong associations.

**The New \*G29A and G1222A of HCRTR1, 5-HTTLPR of SLC6A4 Polymorphisms and Hypocretin-1, Serotonin Concentrations in Migraine Patients.**

[Kowalska M](#)<sup>1</sup>, [Kapelusiak-Pielok M](#)<sup>2</sup>, [Grzelak T](#)<sup>3</sup>, [Wypasek E](#)<sup>4,5,6</sup>, [Kozubski W](#)<sup>2</sup>, [Dorszewska J](#)<sup>1</sup>.

Front Mol Neurosci. **2018 Jun 5**;11:191. doi: 10.3389/fnmol.2018.00191. PMCID: PMC5996111. PMID: 29922128. eCollection 2018.

Migraine is one of the most common primary headache disorders that affects 11% of the adult population. The disease is divided into two main clinical subtypes: migraine with aura (MA) and migraine without aura (MO). Both serotonergic and hypocretinergic systems are involved in the migraine pathomechanism. Polymorphisms in the serotonin transporter gene (*SLC6A4*) and the hypocretin receptor 1 gene (*HCRTR1*) may be risk factors for migraine development due to their ability to affect serotonin and hypocretin-1 (HCRT-1) concentrations. The aim of the study was to analyze, for the first time in the Polish population, the 5-HT transporter linked polymorphic region (5-HTTLPR) in *SLC6A4*, G1222A (rs2271933) and the never before studied \*G29A (rs41263963) polymorphisms in the *HCRTR1* gene, as well as the 5-HT and hypocretin-1 plasma concentrations in migraine patients (MA, MO) and control subjects. The study included 123 patients that were diagnosed with migraine and 123 control subjects. Methods such as PCR, HRMA and sequencing were used for genotyping, while 5-HT was determined by HPLC/EC and hypocretin-1 by ELISA. No significant differences were observed in 5-HTTLPR frequencies. The A allele of *HCRTR1* G1222A occurred more often in MO, while the GA genotype of *HCRTR1* \*G29A was more frequent among MA when compared to control group ( $p < 0.05$ ). The mean age of migraine onset in individuals with *HCRTR1* \*G29A was 18 years old for patients with MA and 26 years old for MO patients. The localization and type of *HCRTR1* polymorphisms (G1222A-missense variant in exon 7, \*G29A-3'UTR variant) may predispose patients to the clinical subtype of migraine: MO or MA, respectively. In control subjects, the short allele of 5-HTTLPR tended to decrease the 5-HT concentration, while the A allele of *HCRTR1* G1222A decreased both 5-HT and hypocretin-1 levels. Serotonin concentrations differed in terms of clinical features of migraine. The relation between genotypes of 5-HTTLPR, *HCRTR1* G1222A, and 5-HT concentrations may be disturbed in migraine. It seems that *HCRTR1* \*G29A is more strongly associated with regulating the 5-HT in patients with MA than MO, and therefore may contribute to the early age of onset for migraine.

## CHRONIC PAIN

[First-in-human randomized clinical trials of the safety and efficacy of tanezumab for treatment of chronic knee osteoarthritis pain or acute bunionectomy pain.](#)

[Walicke PA](#)<sup>1</sup>, [Hefti F](#)<sup>1</sup>, [Bales R](#)<sup>1</sup>, [Lu SP](#)<sup>1</sup>, [Ruckle JL](#)<sup>2</sup>, [Brown MT](#)<sup>3</sup>, [West CR](#)<sup>3</sup>, [Shelton DL](#)<sup>1</sup>.

Pain Rep. 2018 May 9;3(3):e653. doi: 10.1097/PR9.0000000000000653. eCollection 2018 May. PMID: 29922745.

**Introduction:** The neurotrophin nerve growth factor has a demonstrated role in pain transduction and pathophysiology.

**Objectives:** Two randomized, double-blind, placebo-controlled, phase 1 studies were conducted to evaluate safety, tolerability, and analgesic efficacy of single doses of tanezumab, a humanized anti-nerve growth factor monoclonal antibody, in chronic or acute pain.

**Methods:** In the first study (CL001), patients with moderate to severe pain from osteoarthritis (OA) of the knee received a single intravenous infusion of tanezumab (3-1000 µg/kg) or placebo in a dose-escalation (part 1; N = 42) or parallel-arm (part 2; N = 79) study design. The second study (CL002) was a placebo-controlled dose-escalation (tanezumab 10-1000 µg/kg; N = 50) study in patients undergoing bunionectomy surgery.

**Results:** Adverse event rates were generally similar across treatments. Most adverse events were generally mild to moderate in severity and no patients discontinued as a result of adverse events. Adverse events of abnormal peripheral sensation were more common with higher doses of tanezumab (≥100 µg/kg) than with placebo. These were generally mild to moderate in severity. Tanezumab provided up to 12 weeks of effective analgesia for OA knee pain, with statistically significant improvements at doses ≥100 µg/kg ( $P < 0.05$ ). By contrast, no trend for analgesic activity was found when tanezumab was administered 8 to 16 hours before bunionectomy.

**Conclusions:** The demonstration of a favorable safety profile and clinical efficacy in OA pain supports clinical development of tanezumab as a potential treatment for chronic pain conditions.

[Are sleep problems and non-specific health complaints risk factors for chronic pain? A prospective population-based study with 17 year follow-up.](#)

[Nitter AK](#)<sup>1</sup>, [Pripp AH](#)<sup>2</sup>, [Forseth KØ](#)<sup>1,3</sup>.

Scand J Pain. 2017 Dec 29;3(4):210-217. doi: 10.1016/j.sjpain.2012.04.001. PMID: 29913872.

**Introduction:** Chronic musculoskeletal pain represents a significant health problem among adults in Norway. The prevalence of chronic pain can be up to 50% in both genders. However, the prevalence of chronic widespread pain is significantly higher in females than in males. Chronic widespread pain is seen as the end of a continuum of pain. There is rather sparse knowledge about the incidence of pain in initially pain free individuals and the course of self-reported pain over time. Moreover, little is known about risk factors for incidence of chronic pain or prognostic factors for the course of self-reported pain. We believe that such knowledge may contribute to develop strategies for treatment at an early stadium of the pain condition and thereby reduce the prevalence of chronic pain included chronic widespread pain.

**Aims of the Study:** The aims of this study were threefold: (1) to calculate the incidence of self-reported musculoskeletal pain in a female cohort, (2) to describe the course of pain and (3) to investigate whether or not health complaints and sleep problems are predictive factors for onset of pain or prognostic factors for the course of pain.

**Methods:** This is a prospective population-based study of all women between 20 and 50 years who were registered in Arendal, Norway, in 1989 (N = 2498 individuals). A questionnaire about chronic pain (pain >3 months duration in muscles, joints, back or the whole body), modulating factors for pain, sleep problems and seven non-specific health complaints was mailed to all traceable women, in 1990 (N = 2498), 1995 (n = 2435) and 2007 (n = 2261). Of these, 1338 responded on all three occasions. Outcome measures were presence and extent of chronic pain.

**Results:** The prevalence of chronic pain was 57% in 1990 and 61% in 2007. From 1990 to 2007, 53% of the subjects changed pain category. The incidence of chronic pain in initially pain free individuals during follow-up was 44%, whereas the recovery rate was 25%. Impaired sleep quality predicted onset of chronic pain. There was a linear association between the number of health complaints and the incidence of chronic pain in initially pain free individuals. Equivalent results were found for persistence of pain and worsening of pain.

**Conclusion:** The prevalence of chronic pain was rather stable throughout the follow-up period, but the prevalence of chronic widespread pain increased. Individual changes in pain extent occurred frequently. The presence of sleep disturbances and number of health complaints predicted onset, persistence and worsening of pain. Implications Sleep problems must be thoroughly addressed as a possible risk factor for onset or worsening of pain. Elimination of sleep problems in an early phase is an interesting approach in treating chronic pain. More research is needed to illuminate the possible pathogenetic relations between pain, non-specific health complaints, sleep problems and also depression.

## CHRONIC PAIN (Continued)

### [Satisfaction with care after reducing opioids for chronic pain.](#)

[Sharp AL](#)<sup>1</sup>, [Shen E](#), [Wu YL](#), [Wong A](#), [Menchine M](#), [Kanter MH](#), [Gould MK](#).

Am J Manag Care. 2018 Jun 1;24(6):e196-e199. PMID: 29939510.

**OBJECTIVES:** An epidemic of opioid overuse has resulted in nationwide efforts to decrease prescribing, but there is concern that implementing these recommendations will cause patients who are accustomed to opioids for chronic pain to be dissatisfied with care.

**STUDY DESIGN:** Retrospective cohort study of satisfaction scores for patients prescribed opioids for noncancer chronic pain for at least 6 consecutive months from 2009 to 2014.

**METHODS:** We used mixed effects regression to examine the association between opioid dose reduction and the frequency of unfavorable patient satisfaction scores. Subgroup analysis compared the effect of dose reduction on satisfaction scores for encounters between patients and their assigned primary care provider (PCP) versus encounters between patients and an unassigned provider.

**RESULTS:** Included were 2492 encounters involving patients with high-dose chronic opioid use for noncancer pain. A reduction in opioid prescribing occurred in 29% of encounters, and most of these resulted in favorable satisfaction scores (86.4%). After adjustment, the odds of an unfavorable score in the dose reduction group were just marginally higher and not significant (odds ratio [OR], 1.31; 95% CI, 1.00-1.73). Stratified by different encounter types, opioid dose reduction was not associated with unfavorable scores for visits with an assigned PCP (OR, 1.16; 95% CI, 0.79-1.70), but the odds of an unfavorable score were higher for encounters with an unassigned provider (OR, 1.50; 95% CI, 1.01-2.23).

**CONCLUSIONS:** Overall, reducing opioid use for chronic pain is not associated with lower patient satisfaction scores, but encounters with unassigned providers may be associated with slightly lower satisfaction when opioids are reduced.

### [Suicide attempts in chronic pain patients. A register-based study.](#)

[Stenager E](#)<sup>1,2</sup>, [Christiansen E](#)<sup>1,2</sup>, [Handberg G](#)<sup>3</sup>, [Jensen B](#)<sup>4</sup>.

Scand J Pain. 2017 Dec 29;5(1):4-7. doi: 10.1016/j.sjpain.2013.09.001. PMID: 29913656.

**Background:** There are several studies about the relationship between depression and chronic non-malignant pain. These studies have shown that up to 50% of chronic pain patients are suffering from depression. It is, therefore, reasonable to expect that pain patients would also have an increased risk of suicidal behaviour. This problem is not well studied. Since 1990 the Centre for Suicide Research, Odense, Denmark has registered all suicide attempts in patients residing in the Region of Funen, Denmark. The Pain Clinic, Odense University Hospital receives patients with chronic pain from the entire Region of Southern Denmark.

**Purpose:** The purpose of the study has been: To investigate, whether patients treated in the Pain Clinic during the period from 1 January 2004 to 31 December 2009 had an increased risk of suicide attempts compared with the background population.

**Materials and Methods:** The Register for Suicide Attempts (RSA) is a product of the WHO research programme WHO/EURO Multicentre Study on Para suicide. The RSA is a longitudinal person-based register. It contains information about people who have been in contact with the health care system in the County of Funen as a result of a suicide attempt. The Pain Clinic, Odense University Hospital receives patients with non-malignant chronic pain from the Region of Southern Denmark with 1,194,659 inhabitants. Data about age, sex, and time of treatment for patients treated in the Pain Clinic during the period were registered. Time and method of the suicide attempts were registered in the RSA. By registry linkages between the patient registers it was possible to calculate any excess risk of suicide attempts in chronic pain patients in the study period. We used a cohort design and calculated incidence rates (IR) and incidence rate ratios (IRRs) for suicide attempts, based on data from RSA. Poisson Regression analyses were used for calculation of IR and IRR for suicide attempts.

**Results:** In the study period from 1 January 2004 to 31 December 2009 1871 patients residing in the Region of Funen in Denmark were referred to The Pain Clinic. In the patient group 258 suicide attempts in 110 persons were registered. In all 6% of the patient group had attempted suicide. An increased risk of suicide attempts was found in the pain population as the incidence rate ratio (IRR) was 3.76 95% CI (3.22; 4.40). No statistical significant differences between men and women were found.

**Conclusion:** In a chronic non-malignant pain population, referred to a pain clinic, the risk of suicide attempts was increased. Implications It is important to be aware of risk factors for suicidal behaviour, i.e. pain history, depression, anxiety, abuse problems, and social problems when caring for patients with chronic pain. More knowledge and training of the staff caring for chronic pain patients are needed to decrease the risk of suicidal behaviour.

## OTHER RESEARCH OF INTEREST

**[The symptomatology of psychological trauma in the aftermath of war \(1945-1980\): UK army veterans, civilians and emergency responders.](#)**

[Engelbrecht A](#)<sup>1</sup>, [Burdett H](#)<sup>1</sup>, [Silva MJ](#)<sup>2</sup>, [Bhui K](#)<sup>2</sup>, [Jones E](#)<sup>1</sup>.

Psychol Med. 2018 Jun 21:1-8. doi: 10.1017/S0033291718001460. PMID: 29925460. [Epub ahead of print]

**BACKGROUND:** UK veterans suffering from a psychological or psychiatric illness as a consequence of service in the Second World War were entitled to a war pension. Their case files, which include regular medical assessments, are a valuable resource to investigate the nature, distribution and duration of symptoms.

**METHODS:** A standardised form was used to collect data from pension records of a random sample of 500 UK army veterans from the first presentation in the 1940s until 1980. Data were also gathered from 50 civilians and 54 emergency responders with a pension for post-traumatic illness following air-raids.

**RESULTS:** The 10 most common symptoms reported by veterans were anxiety, depression, sleep problems, headache, irritability/anger, tremor/shaking, difficulty completing tasks, poor concentration, repeated fears and avoidance of social contact. Nine of the 10 were widely distributed across the veteran population when symptoms were ranked by the number of subjects who reported them. Nine symptoms persisted significantly longer in the veteran sample than in emergency responders. These included seven of the most common symptoms, together with two others: muscle pain and restlessness. The persistence of these symptoms in the veteran group suggests a post-traumatic illness linked to lengthy overseas service in combat units.

**CONCLUSIONS:** The nature and duration of symptoms exhibited by veterans may be associated with their experience of heightened risks. Exposure to severe or prolonged trauma seems to be associated with chronic multi-symptom illness, symptoms of post-traumatic stress and somatic expressions of pain that may delay or complicate the recovery process.

**[Association of Stress-Related Disorders With Subsequent Autoimmune Disease.](#)**

[Song H](#)<sup>1,2</sup>, [Fang F](#)<sup>2</sup>, [Tomasson G](#)<sup>3,4,5</sup>, [Arnberg FK](#)<sup>6,7</sup>, [Mataix-Cols D](#)<sup>8,9</sup>, [Fernández de la Cruz L](#)<sup>8</sup>, [Almqvist C](#)<sup>2,10</sup>, [Fall K](#)<sup>11,2</sup>, [Valdimarsdóttir UA](#)<sup>1,2,12</sup>.

JAMA. 2018 Jun 19;319(23):2388-2400. doi: 10.1001/jama.2018.7028. PMID: 29922828.

**Importance:** Psychiatric reactions to life stressors are common in the general population and may result in immune dysfunction. Whether such reactions contribute to the risk of autoimmune disease remains unclear.

**Objective:** To determine whether there is an association between stress-related disorders and subsequent autoimmune disease.

**Design, Setting, and Participants:** Population- and sibling-matched retrospective cohort study conducted in Sweden from January 1, 1981, to December 31, 2013. The cohort included 106 464 exposed patients with stress-related disorders, with 1 064 640 matched unexposed persons and 126 652 full siblings of these patients.

**Exposures:** Diagnosis of stress-related disorders, ie, posttraumatic stress disorder, acute stress reaction, adjustment disorder, and other stress reactions.

**Main Outcomes and Measures:** Stress-related disorder and autoimmune diseases were identified through the National Patient Register. The Cox model was used to estimate hazard ratios (HRs) with 95% CIs of 41 autoimmune diseases beyond 1 year after the diagnosis of stress-related disorders, controlling for multiple risk factors.

**Results:** The median age at diagnosis of stress-related disorders was 41 years (interquartile range, 33-50 years) and 40% of the exposed patients were male. During a mean follow-up of 10 years, the incidence rate of autoimmune diseases was 9.1, 6.0, and 6.5 per 1000 person-years among the exposed, matched unexposed, and sibling cohorts, respectively (absolute rate difference, 3.12 [95% CI, 2.99-3.25] and 2.49 [95% CI, 2.23-2.76] per 1000 person-years compared with the population- and sibling-based reference groups, respectively). Compared with the unexposed population, patients with stress-related disorders were at increased risk of autoimmune disease (HR, 1.36 [95% CI, 1.33-1.40]). The HRs for patients with posttraumatic stress disorder were 1.46 (95% CI, 1.32-1.61) for any and 2.29 (95% CI, 1.72-3.04) for multiple (≥3) autoimmune diseases. These associations were consistent in the sibling-based comparison. Relative risk elevations were more pronounced among younger patients (HR, 1.48 [95% CI, 1.42-1.55]; 1.41 [95% CI, 1.33-1.48]; 1.31 [95% CI, 1.24-1.37]; and 1.23 [95% CI, 1.17-1.30] for age at ≤33, 34-41, 42-50, and ≥51 years, respectively; P for interaction < .001). Persistent use of selective serotonin reuptake inhibitors during the first year of posttraumatic stress disorder diagnosis was associated with attenuated relative risk of autoimmune disease (HR, 3.64 [95% CI, 2.00-6.62]; 2.65 [95% CI, 1.57-4.45]; and 1.82 [95% CI, 1.09-3.02] for duration ≤179, 180-319, and ≥320 days, respectively; P for trend = .03).

**Conclusions and Relevance:** In this Swedish cohort, exposure to a stress-related disorder was significantly associated with increased risk of subsequent autoimmune disease, compared with matched unexposed individuals and with full siblings. Further studies are needed to better understand the underlying mechanisms.

## OTHER RESEARCH OF INTEREST (Continued)

[Disability Rating, Age at Death, and Cause of Death in U.S. Veterans with Service-Connected Conditions.](#)[Maynard C](#)<sup>1,2</sup>, [Trivedi R](#)<sup>3,4</sup>, [Nelson K](#)<sup>1,2,5</sup>, [Fihn SD](#)<sup>1,2,5,6</sup>.

Mil Med. 2018 Mar 26. doi: 10.1093/milmed/usy040. PMID: 29590473. [Epub ahead of print]

**Introduction:** The association between disability and cause of death in Veterans with service-connected disabilities has not been studied. The objective of this study was to compare age at death, military service and disability characteristics, including disability rating, and cause of death by year of birth. We also examined cause of death for specific service-connected conditions.

**Materials and Methods:** This study used information from the VETSNET file, which is a snapshot of selected items from the Veterans Benefits Administration corporate database. We also used the National Death Index (NDI) for Veterans which is part of the VA Suicide Data Repository. In VETSNET, there were 758,324 Veterans who had a service-connected condition and died between the years 2004 and 2014. Using the scrambled social security number to link the two files resulted in 605,493 (80%) deceased Veterans. Age at death, sex, and underlying cause of death were obtained from the NDI for Veterans and military service characteristics and types of disability were acquired from VETSNET. We constructed age categories corresponding to period of service; birth years 1938 and earlier corresponded to Korea and World War II ("oldest"), birth years 1939-1957 to the Vietnam era ("middle"), and birth years 1958 and later to post Vietnam, Gulf War, and the more recent conflicts in Iraq and Afghanistan ("youngest").

**Results:** Sixty-two percent were in the oldest age category, 34% in the middle group, and 4% in the youngest one. The overall age at death was 75 ± 13 yr. Only 1.6% of decedents were women; among women 25% were in the youngest age group, while among men only 4% were in the youngest group. Most decedents were enlisted personnel, and 60% served in the U.S. Army. Nearly 61% had a disability rating of >50% and for the middle age group 54% had a disability rating of 100%. The most common service-connected conditions were tinnitus, hearing loss, and post-traumatic stress disorder (PTSD). In the oldest group, nearly half of deaths were due to cancer or cardiovascular conditions and <2% were due to external causes. In the youngest group, cardiovascular disease and cancer accounted for about 1/3 of deaths, whereas external causes or deaths due to accidents, suicide, or assault accounted for nearly 33% of deaths. For Veterans with service-connected PTSD or major depression; 6.5% of deaths were due to external causes whereas for Veterans without these conditions, only 3.1% were due to external causes.

**Conclusion:** The finding of premature death due to external causes in the youngest age group as well as the finding of higher proportions of external causes in those with PTSD or major depression should be of great concern to those who care for Veterans.

[Veteran-centred content in medical education.](#)[Ross PT](#)<sup>1</sup>, [Lypson ML](#)<sup>1,2</sup>.

Clin Teach. 2018 Mar 30. doi: 10.1111/tct.12775. PMID: 29600591. [Epub ahead of print]

**BACKGROUND:** Veterans have unique experiences that warrant special consideration in health care. Unfortunately, training in veteran-centred care has not been a clear focus of medical education, and only a very small proportion of medical schools include military cultural competency in their curricula.

**METHODS:** We conducted an 80-minute focus group with six US veterans. Open-ended questions were used to elicit their perceptions of the health care that they receive, and how it can be improved. The audio-recording was transcribed verbatim and coded for thematic content. A phenomenological analytic approach was used to analyse the 31-page transcript and arrive at the final themes.

**RESULTS:** Former service members from various periods of conflict (e.g. World War II, Vietnam, Persian Gulf) offered key insights about how to improve veterans' health care experiences. Veterans suggested that consideration of their previous military service would improve care. They lamented that the lack of military consciousness is a barrier to care. Finally, they suggested that clinicians pay close attention to the transition from service member to civilian, as reintegration to civilian life is a critical life experience. Training in veteran-centred care has not been a clear focus of medical education

**DISCUSSION:** Veteran-centred care ensures optimal health care through ease of access to services, and through positive patient-provider interactions. Being aware of military culture can help providers to contextualise veterans' experiences and beliefs about health care seeking and illness management, particularly for invisible wounds of war, including traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD).