

GULF WAR ILLNESS

[Autonomic Symptoms in Gulf War Veterans Evaluated at the War Related Illness and Injury Study Center.](#)

[Fox A](#)¹, [Helmer D](#)^{1,2}, [Tseng CL](#)¹, [McCarron K](#)¹, [Satcher S](#)¹, [Osinubi O](#)¹.

Mil Med. 2018 Sep 12. doi: 10.1093/milmed/usy227. PMID: 30215755. [Epub ahead of print]

Introduction: We characterized the presence of autonomic symptoms in a sample of Veterans with Gulf War Illness (GWI) using the Composite Autonomic Symptom Scale (COMPASS-31). In addition, we examined the report of autonomic symptoms across comorbid mental health conditions in this sample.

Materials and Methods: Case-series follow-up of Gulf War veterans evaluated by the War Related Illness and Injury Study Center (WRIISC) between 2011 and 2016 (n = 153). Phone-based interview consisted of questionnaires designed to investigate autonomic symptoms, physical symptoms, mental health conditions, and GWI. Sixty-One Veterans agreed to participate in this follow-up arm of the study. We restricted our analysis to only those Veterans meeting CDC and/or Kansas criteria for GWI, leaving us with a sample of 56 Veterans.

Results: Veterans in our sample were, male (n = 55, 98%), 49 (±6.8) years old and used 8 (±6.6) medications. The mean COMPASS-31 score for our sample was 45.6 (±18.3). There were no differences in reports of autonomic symptoms between participants who screened positive or negative for depression or post-traumatic stress disorder, but COMPASS-31 scores were higher among those who screened positive for anxiety (49.6 (±16.0)) compared with those who screened negative (29.3 (±18.9)) (p < 0.001).

Conclusions: The elevated COMPASS-31 scores suggest that there may be autonomic dysfunction present in our sample of Veterans with GWI, consistent with other published reports. Additionally, we believe that the high scores on the anxiety measure may reflect assessment of physiological symptoms that are not specific to anxiety, and may reflect GWI symptoms. Objective physiological tests of the autonomic nervous system are warranted to better characterize autonomic function and the clinical relevance of COMPASS-31 in this population.

CHRONIC FATIGUE SYNDROME

[Pitfalls in cytokine measurements - Plasma TGF-β1 in chronic fatigue syndrome.](#)

[Roerink ME](#)¹, [van der Schaaf ME](#), [Hawinkels LJAC](#), [Raijmakers RPH](#), [Knoop H](#), [Joosten LAB](#), [van der Meer JWM](#).

Neth J Med. 2018 Sep;76(7):310-313. PMID: 30220655.

BACKGROUND: Serum TGF-β1 concentrations are reported to be elevated in chronic fatigue syndrome (CFS). However, measurement of circulating cytokines is a complex procedure and control of pre-analytical procedures is essential. The objective of the current study was to measure circulating TGF-β1 concentrations in CFS patients compared to healthy controls, taking into account differences in pre-analytical procedures.

METHODS: Two cohorts of female CFS patients were included. In both studies patients were asked to bring a healthy, age-matched control. At baseline, TGF-β1 levels were measured in plasma and additionally P-selectin, a marker of platelet activity, was determined in a subgroup of participants.

RESULTS: 50 patients and 48 controls were included in cohort I, and 90 patients and 29 controls in cohort II. Within the cohorts there were no differences in TGF-β1 concentrations. However, between the cohorts there was a large discrepancy, which appeared to be caused by differences in g-force of the centrifuges used. The lower g-force used in cohort II (1361 g) caused more platelet activation, reflected by higher p-selectin concentrations, compared to cohort I (p < 0.0001), which was confirmed in a second independent experiment. There was a correlation between TGF-β1 and p-selectin concentrations (r 0.79, p < 0.0001).

CONCLUSION: These results demonstrate that control of pre-analytical procedures is an essential aspect when measuring circulating cytokines. No evidence for enhanced TGF-β1 in patients with CFS was found.

CHRONIC FATIGUE SYNDROME (Continued)

[Why do some ME/CFS patients benefit from treatment with sodium dichloroacetate, but others do not?](#)

[Comhaire F¹](#).

Med Hypotheses. **2018 Nov**;120:65-67. doi: 10.1016/j.mehy.2018.08.014. PMID: 30220343. Epub 2018 Aug 25.

Myalgic Encephalopathy/Chronic Fatigue Syndrome (ME/CFS) is an enigmatic disease the pathogenesis of which remains elusive. Pragmatic proof-of-principle of the hypothetical mechanisms causing the clinical symptoms has been delivered, but it is hard to explain why some patients do respond favourably to treatment with sodium dichloroacetate (DCA), which enhances the activity of the mitochondrial enzyme pyruvate dehydrogenase, but other patients experience no benefit from this substance. In a prospective trial including 35 ME/CFS patients, logistic regression analysis with stepwise elimination has identified 6 pre-treatment characteristics allowing for the differentiation between responders (n = 13) and non-responders (n = 22) with high accuracy (P < 0.0001; area under the ROC-curve = 0.92). A formula was derived generating the probability of belonging to the group of responders. This finding may assist in selecting ME/CFS patients suitable for treatment with DCA, but requires further studies as to the predictive capacity of the derived formula.

[Chronic fatigue syndrome patients have alterations in their oral microbiome composition and function.](#)

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PLoS One. **2018 Sep 11**;13(9):e0203503. doi: 10.1371/journal.pone.0203503. PMID: 30204780. eCollection 2018.

Host-microbe interactions have been implicated in the pathogenesis of chronic fatigue syndrome (CFS), but whether the oral microbiome is altered in CFS patients is unknown. We explored alterations of the oral microbiome in Chinese Han CFS patients using 16S rRNA gene sequencing and alterations in the functional potential of the oral microbiome using PICRUSt. We found that Shannon and Simpson diversity indices were not different in CFS patients compared to healthy controls, but the overall oral microbiome composition was different (MANOVA, p < 0.01). CFS patients had a higher relative abundance of Fusobacteria compared with healthy controls. Further, the genera Leptotrichia, Prevotella, and Fusobacterium were enriched and Haemophilus, Veillonella, and Porphyromonas were depleted in CFS patients compared to healthy controls. Functional analysis from inferred metagenomes showed that bacterial genera altered in CFS patients were primarily associated with amino acid and energy metabolism. Our findings demonstrate that the oral microbiome in CFS patients is different from healthy controls, and these differences lead to shifts in functional pathways with implications for CFS pathogenesis. These findings increase our understanding of the relationship between the oral microbiota and CFS, which will advance our understanding of CFS pathogenesis and may contribute to future improvements in treatment and diagnosis.

HEADACHE and MIGRAINE

[Survey Analysis of the Use, Effectiveness, and Patient-Reported Tolerability of Inhaled Oxygen Compared With Injectable Sumatriptan for the Acute Treatment of Cluster Headache.](#)

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Headache. 2018 Sep 17. doi: 10.1111/head.13405. PMID: 30221765. [Epub ahead of print]

OBJECTIVE: In this secondary analysis of the Clusterbusters® Medication Use survey, the use, effectiveness, and tolerability of inhaled oxygen were investigated and compared with injectable sumatriptan. We also sought to understand the predictors of medication response.

BACKGROUND: Inhaled oxygen is a mainstay abortive intervention in cluster headache but is not approved by the Food and Drug Administration (FDA). Unlike injectable sumatriptan, the only FDA-approved pharmacologic intervention for cluster headache, oxygen can be used multiple times a day, which is highly relevant for a condition with numerous daily attacks. In addition to obstacles in obtaining oxygen therapy, optimal oxygen delivery (ie, mask, flow rate) is not uniformly employed in cluster headache. These factors lead to underuse and imprecise therapeutic response rates.

METHODS: A secondary analysis was conducted using deidentified data from the Clusterbusters® Medication Use survey, which was modeled after previously published surveys and available online. Subjects were recruited from headache clinics and cluster headache websites. Most responses were chosen from a list; others were free-texted. The final analysis included responses from 493 adult participants with a validated diagnosis of cluster headache. This analysis of deidentified data from the Clusterbusters® Medication Use survey received institutional approval.

RESULTS: The most commonly used delivery system used by subjects was a non-rebreather-type mask. The use of oxygen flow rates >10 L/min was a positive predictor of medication response (OR = 2.36, P = .016). Among those who used flow rates >10 L/min, both inhaled oxygen (81.5%) and injectable sumatriptan (80.5%) were efficacious and did not differ significantly from each other in any specific group examined. At flow rates >10 L/min, positive predictors of oxygen response were male gender (OR = 2.07, P = .031) and cigarette smoking (current or historical; OR = 2.25, P = .017). Among the groups examined, there were no predictors of sumatriptan response. Most comments about side effects and concerns were directed at triptans.

CONCLUSION: Therapeutic response to inhaled oxygen at sufficiently high flow rates (>10 L/min) had comparable efficacy to that of injectable sumatriptan for the acute treatment of cluster headache. Other factors in oxygen delivery (ie, flow rate changes) should be explored for optimization of therapy. The reasons for improved oxygen response in males and those with a cigarette smoking history require further exploration. While both oxygen and sumatriptan can be effective in the management of cluster headache, patient-reported side effects and concerns were more commonly directed at triptan medications. Current restrictions on access to inhaled oxygen, which exist at many levels, limit the therapeutic options available for patients with cluster headache, thereby doing a disservice to this patient population and the providers who deliver their care.

HEADACHE and MIGRAINE (Continued)

[Patients' perspective on the burden of migraine in Europe: a cross-sectional analysis of survey data in France, Germany, Italy, Spain, and the United Kingdom.](#)

[Vo P](#)¹, [Fang J](#)², [Bilitou A](#)³, [Laflamme AK](#)¹, [Gupta S](#)⁴.

J Headache Pain. **2018 Sep 10**;19(1):82. doi: 10.1186/s10194-018-0907-6. PMID: 30203163.

BACKGROUND: Migraine is a distinct neurological disease that imposes a significant burden on patients, society, and the healthcare system. This study aimed to characterize the incremental burden of migraine in individuals who suffer from ≥ 4 monthly headache days (MHDs) by examining health-related quality of life (HRQoL), impairments to work productivity and daily activities, and healthcare resource utilization (HRU) in the EU5 (France, Germany, Italy, Spain, United Kingdom).

METHODS: This retrospective cross-sectional study used data from the 2016 National Health and Wellness Survey (NHWS; N = 80,600). Short-Form 36-Item Health Survey, version 2 (SF-36v2) physical and mental component summary scores (PCS and MCS), Short-form-6D (SF-6D), and EuroQoL (EQ-5D), impairments to work productivity and daily activities (Work Productivity and Activity Impairment Questionnaire (WPAI), and HRU were compared between migraine respondents suffering from ≥ 4 MHDs (n = 218) and non-migraine controls (n = 218) by propensity score matching using sociodemographic characteristics. Chi-square, T-tests, and Mann-Whitney tests were performed to determine significant differences between the groups after propensity score matching.

RESULTS: HRQoL was lower in migraine individuals suffering from ≥ 4 MHDs compared with non-migraine controls, with reduced SF-36v2 PCS (46.00 vs 50.51) and MCS (37.69 vs 44.82), SF-6D health state utility score (0.62 vs 0.71), and EQ-5D score (0.68 vs 0.81) (for all, $p < 0.001$). Respondents with migraine suffering from ≥ 4 MHDs also reported higher levels of absenteeism from work (14.43% vs 9.46%; $p = 0.001$), presenteeism (35.52% vs 20.97%), overall work impairment (38.70% vs 23.27%), and activity impairment (44.17% vs 27.75%) than non-migraine controls (for all, $p < 0.001$). Additionally, HRU was significantly higher for individuals with ≥ 4 MHDs compared to their matched controls. Consistently, migraine subgroups (4-7 MHDs, 8-14 MHDs and CM) had lower HRQoL, greater overall work and activity impairment, and higher HRU compared to non-migraine controls.

CONCLUSIONS: Migraine of ≥ 4 MHDs was associated with poorer HRQoL, greater work productivity loss, and higher HRU compared with non-migraine controls. The findings of the study suggest that an unmet need exists among individuals suffering from ≥ 4 MHDs in the EU5 suggesting the need for effective prophylactic treatments to lessen the humanistic and economic burden of migraine.

[Risk and Predisposing Factors for Suicide Attempts in Patients with Migraine and Status Migrainosus: A Nationwide Population-Based Study.](#)

[Harnod T](#)^{1,2}, [Lin CL](#)^{3,4}, [Kao CH](#)^{5,6,7}.

J Clin Med. **2018 Sep 11**;7(9). pii: E269. doi: 10.3390/jcm7090269. PMID: 30208570.

OBJECTIVE: To investigate the risk and risk factors for suicide attempt by patients with regular migraines (RM) and status migrainosus (SM) in Taiwan.

METHODS: We analyzed a subset of the National Health Insurance Research Database of Taiwan and enrolled patients (≥ 20 years old) who had ever received a diagnosis of RM or SM between 2000 and 2012 in the RM and SM cohort. The SM cohort included 13,605 patients, the RM cohort had 21,485 patients, and the comparison cohort contained approximately four times that many patients. We calculated the adjusted hazard ratios and 95% confidence intervals (CI) for suicide attempts after adjusting for age, sex, monthly income, urbanization level, occupation, and comorbidities.

RESULTS: The SM cohort had a 1.81-fold risk of attempting suicide (95% CI = 1.14-2.89) compared to the comparison cohort. Other factors that predispose patients with SM to attempt suicide include the following: female sex, relatively young age (< 50 years old), and low monthly income ($< 15,000$ New Taiwan Dollars, approximately equivalent to 495 US Dollars). Additionally, the risk of attempting suicide only increased in patients who had been diagnosed with SM for longer than five years.

CONCLUSION: SM is associated with a higher risk for suicide attempt in migraineurs in Taiwan. This finding is important to clinicians and government officials seeking to prevent patients from attempting suicide in Taiwan and other similar East Asian countries.

HEADACHE and MIGRAINE (Continued)

[Impact of migraine on the clinical presentation of insomnia: a population-based study.](#)

[Kim J¹](#), [Cho SJ²](#), [Kim WJ³](#), [Yang KI⁴](#), [Yun CH⁵](#), [Chu MK⁶](#).

J Headache Pain. 2018 Sep 14;19(1):86. doi: 10.1186/s10194-018-0916-5. PMID: 30218221.

BACKGROUND: Insomnia and migraine are closely related; insomnia aggravates migraine symptoms. This study was conducted to investigate the impact of migraine on the clinical presentation of insomnia symptoms.

METHODS: The data of the Korean Headache-Sleep Study (KHSS) were used in the present study. The KHSS is a nation-wide cross-sectional population-based survey regarding headache and sleep in Korean adults aged 19 to 69 years. If a participant's Insomnia Severity Index (ISI) score ≥ 10 , she/he was classified as having insomnia. The clinical presentation of insomnia symptoms was assessed using total and subcomponent scores of the ISI.

RESULTS: Of 2695 participants, 290 (10.8%) and 143 (5.3%) individuals were assigned as having insomnia and migraine, respectively. The proportions of migraine (12.8% vs. 4.4%, $p < 0.001$) and non-migraine headache (59.0% vs. 39.9%, $p < 0.001$) were higher among individuals with insomnia compared to those without insomnia. Among participants with insomnia, total ISI scores were not significantly different among participants with migraine, non-migraine, and non-headache [median and interquartile range: 13.0 (11.0-17.5) vs. 13.0 (11.0-17.5) vs. 12.0 (11.0-16.0), $p = 0.245$]. ISI scores for noticeability of sleep problems to others were significantly higher among participants with migraine [3.0 (2.0-4.0) vs. 2.0 (2.0-3.0), $p = 0.011$] and non-migraine headache [3.0 (2.0-4.0) vs. 2.0 (2.0-3.0), $p = 0.001$] compared to those without headache history. Other ISI subcomponent scores did not significantly differ between headache status groups.

CONCLUSIONS: Participants with insomnia had an increased risk of migraine and non-migraine headache compared to those without insomnia. Among participants with insomnia, overall insomnia severity was not significantly influenced by the headache status.

[A prospective pilot study of the effect on catecholamines of mindfulness training vs pharmacological prophylaxis in patients with chronic migraine and medication overuse headache.](#)

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Cephalalgia. 2018 Sep 13;333102418801584. doi: 10.1177/0333102418801584. PMID: 30213202. [Epub ahead of print]

Aim: To address whether, in patients with chronic migraine and medication overuse headache, mindfulness-based treatment is associated with changes in plasma levels of catecholamines and elusive amines that are similar to those observed in patients undergoing pharmacological prophylaxis.

Methods: In this non-randomized, clinic-based effectiveness study, patients aged 18-65, with a history of chronic migraine ≥ 10 years and overuse of triptans or non-steroidal anti-inflammatory drugs ≥ 5 years, were enrolled. Upon completion of a structured withdrawal program, patients received either pharmacological prophylaxis or six weekly sessions of mindfulness-based treatment and were followed for 12 months. Daily headache diaries were used to record headache frequency and medication intake; catecholamines (noradrenaline, epinephrine and dopamine) and levels of elusive amines were assayed from poor platelet plasma.

Results: Complete follow-up data were available for 15 patients in the pharmacological prophylaxis-group (14 females, average age 44.1) and 14 in the mindfulness treatment-group (all females, average age 46.4), and all variables were comparable between groups at baseline. At 12 months, significant improvement ($p < .001$) was found in the pharmacological prophylaxis group for headache frequency and medication intake (by 51% and 48.7%, respectively), noradrenaline, epinephrine and dopamine (by 98.7%, 120.8% and 501.9%, respectively); patients in the mindfulness treatment-group performed similarly. For elusive amines, no longitudinal changes were found.

Conclusions: The similar improvement trends observed in the two groups of patients further support the utility of mindfulness-based treatment in migraine care, and reinforce the hypothesis that alteration and normalization of tyrosine metabolism are implicated in migraine chronification and in remission of chronic migraine.

CHRONIC PAIN

[Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults - United States, 2016.](#)

[Dahlhamer J](#), [Lucas J](#), [Zelaya C](#), [Nahin R](#), [Mackey S](#), [DeBar L](#), [Kerns R](#), [Von Korff M](#), [Porter L](#), [Helmick C](#).

MMWR Morb Mortal Wkly Rep. **2018 Sep 14**;67(36):1001-1006. doi: 10.15585/mmwr.mm6736a2. PMID: 30212442.

Chronic pain, one of the most common reasons adults seek medical care (1), has been linked to restrictions in mobility and daily activities (2,3), dependence on opioids (4), anxiety and depression (2), and poor perceived health or reduced quality of life (2,3). Population-based estimates of chronic pain among U.S. adults range from 11% to 40% (5), with considerable population subgroup variation. As a result, the 2016 National Pain Strategy called for more precise prevalence estimates of chronic pain and high-impact chronic pain (i.e., chronic pain that frequently limits life or work activities) to reliably establish the prevalence of chronic pain and aid in the development and implementation of population-wide pain interventions (5). National estimates of high-impact chronic pain can help differentiate persons with limitations in major life domains, including work, social, recreational, and self-care activities from those who maintain normal life activities despite chronic pain, providing a better understanding of the population in need of pain services. To estimate the prevalence of chronic pain and high-impact chronic pain in the United States, CDC analyzed 2016 National Health Interview Survey (NHIS) data. An estimated 20.4% (50.0 million) of U.S. adults had chronic pain and 8.0% of U.S. adults (19.6 million) had high-impact chronic pain, with higher prevalences of both chronic pain and high-impact chronic pain reported among women, older adults, previously but not currently employed adults, adults living in poverty, adults with public health insurance, and rural residents. These findings could be used to target pain management interventions.

[Chronic Pain Among Suicide Decedents, 2003 to 2014: Findings From the National Violent Death Reporting System.](#)

[Petrosky E](#)¹, [Harpaz R](#)¹, [Fowler KA](#)¹, [Bohm MK](#)¹, [Helmick CG](#)¹, [Yuan K](#)¹, [Betz CJ](#)¹.

Ann Intern Med. **2018 Sep 11**. doi: 10.7326/M18-0830. PMID: 30208405. Epub ahead of print]

Background: More than 25 million adults in the United States have chronic pain. Chronic pain has been associated with suicidality, but previous studies primarily examined nonfatal suicidal behaviors rather than suicide deaths associated with chronic pain or the characteristics of such deaths.

Objective: To estimate the prevalence of chronic pain among suicide decedents in a large multistate sample and to characterize suicide decedents with and without chronic pain.

Design: Retrospective analysis of National Violent Death Reporting System (NVDRS) data. The NVDRS links death certificate, coroner or medical examiner, and law enforcement data collected by investigators, who often interview informants who knew the decedent to gather information on precipitating circumstances surrounding the suicide. Information is abstracted by using standard coding guidance developed by the Centers for Disease Control and Prevention.

Setting: 18 states participating in the NVDRS.

Participants: Suicide decedents with and without chronic pain who died during 1 January 2003 to 31 December 2014.

Measurements: Demographic characteristics, mechanism of death, toxicology results, precipitating circumstances (mental health, substance use, interpersonal problems, life stressors), and suicide planning and intent.

Results: Of 123 181 suicide decedents included in the study, 10 789 (8.8%) had evidence of chronic pain, and the percentage increased from 7.4% in 2003 to 10.2% in 2014. More than half (53.6%) of suicide decedents with chronic pain died of firearm-related injuries and 16.2% by opioid overdose.

Limitation: The results probably underrepresent the true percentage of suicide decedents who had chronic pain, given the nature of the data and how they were captured.

Conclusion: Chronic pain may be an important contributor to suicide. Access to quality, comprehensive pain care and adherence to clinical guidelines may help improve pain management and patient safety.

Primary Funding Source: None.

CHRONIC PAIN (Continued)

[Associations of catechol-O-methyltransferase \(rs4680\) Single Nucleotide Polymorphisms with Opioid Use and Dose Among Adults with Chronic Pain.](#)

[Hooten WM](#)¹, [Biernacka JM](#)², [O'Brien TG](#)³, [Cunningham JM](#)⁴, [Black JL](#)⁴.

Pain. **2018 Sep 11**. doi: 10.1097/j.pain.0000000000001400. PMID: 30211780. [Epub ahead of print]

Catechol-O-methyltransferase (COMT) regulates extracellular catecholamines. A widely studied COMT single nucleotide polymorphism (rs4680) changes the translated amino acid from valine to methionine (Val158Met); the polymorphism has been shown to influence opioid use. The aims of this study were to investigate the influence of COMT Val158Met on the likelihood and dose of opioid use in adults with chronic pain. Adults with chronic pain consecutively admitted to an outpatient pain rehabilitation program were recruited for study participation (N=298). Individuals were genotyped for COMT Val158Met (rs4680). The polymorphism was analyzed using an additive and codominant genotype model. The distribution of genotypes was 23% (N=70) for Val/Val, 49% (N=146) for Val/Met, and 27% (N=82) for Met/Met (Hardy-Weinberg, $P > .90$). No significant association was observed between opioid use and genotype under the additive model; however, a significant association was observed under the codominant model ($P = 0.027$). A post-hoc comparison demonstrated that the Met/Met genotype was more likely to use opioids compared to the Val/Met genotype ($P = 0.0089$). No significant association was observed between morphine equivalent dose (MED) and genotype under the additive model; however, a significant association was observed under the codominant model ($P = 0.0496$) (Table 2). A post-hoc comparison demonstrated that the Val/Met ($P = 0.019$) and Met/Met ($P = 0.043$) genotypes used greater MED compared to the Val/Val genotype. This study extends key knowledge about the influence of the Met/Met genotype and Met allele on opioid use in adults with chronic pain.

[Impact of Cigarette Smoking Status on Pain Intensity Among Veterans With and Without Hepatitis C.](#)

[Lynch SM](#)¹, [Wilson SM](#)^{2,3}, [DeRycke EC](#)⁴, [Driscoll MA](#)^{4,5}, [Becker WC](#)^{4,6}, [Goulet JL](#)^{4,7}, [Kerns RD](#)⁶, [Mattocks KM](#)^{8,9}, [Brandt CA](#)^{4,7}, [Bathulapalli H](#)⁴, [Skanderson M](#)⁴, [Haskell SG](#)^{4,6}, [Bastian LA](#)^{4,6}.

Pain Med. **2018 Sep 1**;19(suppl_1):S5-S11. doi: 10.1093/pm/pny146. PMID: 30203017.

Objective: Chronic pain is a significant problem in patients living with hepatitis C virus (HCV). Tobacco smoking is an independent risk factor for high pain intensity among veterans. This study aims to examine the independent associations with smoking and HCV on pain intensity, as well as the interaction of smoking and HCV on the association with pain intensity.

Design/Participants: Cross-sectional analysis of a cohort study of veterans of Operations Enduring Freedom/Iraqi Freedom/New Dawn (OEF/OIF/OND) who had at least one visit to a Veterans Health Administration (VHA) primary care clinic between 2001 and 2014.

Methods: HCV was identified using ICD-9 codes from electronic medical records (EMRs). Pain intensity, reported on a 0-10 numeric rating scale, was categorized as none/mild (0-3) and moderate/severe (4-10).

Results: Among 654,841 OEF/OIF/OND veterans (median age [interquartile range] = 26 [23-36] years), 2,942 (0.4%) were diagnosed with HCV. Overall, moderate/severe pain intensity was reported in 36% of veterans, and 37% were current smokers. The adjusted odds of reporting moderate/severe pain intensity were 1.23 times higher (95% confidence interval [CI] = 1.14-1.33) for those with HCV and 1.26 times higher (95% CI = 1.25-1.28) for current smokers. In the interaction model, there was a significant Smoking Status × HCV interaction ($P = 0.03$). Among veterans with HCV, smoking had a significantly larger association with moderate/severe pain (adjusted odds ratio [OR] = 1.50, $P < 0.001$) than among veterans without HCV (adjusted OR = 1.26, $P < 0.001$).

Conclusions: We found that current smoking is more strongly linked to pain intensity among veterans with HCV. Further investigations are needed to explore the impact of smoking status on pain and to promote smoking cessation and pain management in veterans with HCV.

CHRONIC PAIN (Continued)

[Mental and Physical Health Correlates of Pain Treatment Utilization Among Veterans With Chronic Pain: A Cross-sectional Study.](#)

[Harding K](#)¹, [Day MA](#)², [Ehde DM](#)³, [Wood AE](#)⁴, [McCall A](#)¹, [Williams R](#)¹.

Mil Med. 2018 Sep 12. doi: 10.1093/milmed/usy235. PMID: 30215759. [Epub ahead of print]

Introduction: The annual cost of treatment and lost productivity due to chronic pain is estimated to be \$635 billion within the USA. Self-management treatments for chronic pain result in lower health care costs and lower utilization of provider-management treatments, such as hospitalization and medication use. The current study sought to identify and characterize patient factors and health conditions associated with chronic pain treatment utilization to inform ways to improve engagement in self-management pain treatment (e.g., applying heat or ice, exercising, or practicing relaxation). This study predicted (1) greater pain intensity and pain interference would be associated with greater utilization of self-management treatments and (2) this association would be moderated by patient factors (gender and age) and health comorbidities (anxiety, trauma, depression, and sleep disturbance).

Materials and Methods: Baseline data from a three-arm clinical trial were collected for 127 Veterans seeking treatment for chronic pain. Veterans were recruited via clinician referral and medical record review at the Veterans Affairs Puget Sound Health Care System, Washington, USA.

Results: Self-management treatments were more utilized than provider-management treatments. Pain intensity and pain interference were not uniquely associated with provider-management or self-management treatment utilization after controlling for demographics and mental health status. Sleep disturbance moderated the relationship between pain interference and provider-management treatment utilization. Depression moderated the relationship between pain intensity and provider-management treatment utilization.

Conclusions: While study conclusions may not generalize to all Veteran populations, findings suggest that Veterans with chronic pain were more likely to seek provider-management treatments when experiencing high-pain interference and high-sleep disturbance. In addition, Veterans were more likely to seek provider-management treatments when experiencing low-pain intensity and high-depression symptoms.

OTHER RESEARCH OF INTEREST

[The Association Between Alcohol Consumption, Lifetime Alcohol Use Disorder, and Psychiatric Distress Among Male and Female Veterans.](#)

[Wilson SM](#)^{1,2,3}, [Burroughs TK](#)⁴, [Newins AR](#)⁵, [Dedert EA](#)^{2,3,6}, [Medenblik AM](#)³, [McDonald SD](#)⁷, [Beckham JC](#)^{2,3,6}; VA Mid-Atlantic MIRECC Workgroup, [Calhoun PS](#)^{1,2,3}.

J Stud Alcohol Drugs. 2018 Jul;79(4):591-600. PMCID: PMC6082130. PMID: 30079875.

OBJECTIVE: This study aimed to examine among veterans (a) whether alcohol consumption patterns are associated with probability of psychiatric symptoms and (b) whether an alcohol use disorder (AUD) history explains psychiatric symptoms among nondrinkers.

METHOD: Data were collected from 3,003 veterans (20.5% women). Gender-stratified logistic models examined the association between alcohol consumption pattern and the odds of symptoms of posttraumatic stress disorder (PTSD), depression, and suicidality. Two types of models were tested: four-group models comparing moderate drinkers to nondrinkers, light, and heavy drinkers; and five-group models separating nondrinkers by AUD history.

RESULTS: In four-group models for both genders, compared with moderate drinkers, hazardous drinkers were more likely to have psychiatric symptoms. Among men, nondrinkers were more likely to have symptoms of depression and suicidality but not PTSD. Among women, nondrinkers and light drinkers were more likely to have PTSD symptoms. In the five-group model for men, odds of symptoms were higher for nondrinkers with an AUD history and hazardous drinkers. Compared to nondrinkers without an AUD history and light drinkers, male nondrinkers with an AUD history had higher odds of psychiatric symptoms. In the five-group model for women, the odds of symptoms were higher for hazardous drinkers. Female nondrinkers with an AUD history had higher odds of a positive depression screen. Odds of a positive PTSD screen were higher for female nondrinkers (with and without an AUD history) and light drinkers.

CONCLUSIONS: For male veterans, there was a protective effect of moderate drinking (compared with abstinence) that disappeared when nondrinkers without an AUD history were separated. However, results for women showed a protective effect of moderate drinking with regard to PTSD that persisted even when an AUD history was taken into account.

OTHER RESEARCH OF INTEREST (Continued)**[Psychosocial Factors that Shape Substance Abuse and Related Mental Health of Women Military Veterans who Use Community-Based Services.](#)**

[Evans EA](#)^{1,2}, [Glover DL](#)², [Washington DL](#)^{2,3}, [Hamilton AB](#)^{2,4}.

Subst Use Misuse. **2018 Sep 19**;53(11):1878-1892. doi: 10.1080/10826084.2018.1441309. PMID: 29485302. Epub 2018 Feb 27.

BACKGROUND: Women Veterans who use the Veterans Health Administration (VA) have high rates of substance abuse and poorer health than non-Veteran women. Less is known about the psychosocial needs of women Veterans who seek care in non-VA settings.

OBJECTIVES: We provide a grounded description of factors that impact substance abuse, mental health, and related quality of life of women Veterans who use non-VA community-based health and social services.

METHODS: Utilizing a mixed methods design, we conducted semi-structured in-person interviews with 22 women Veterans in Los Angeles in 2013-2015.

RESULTS: The current health of these women Veterans was shaped by substance abuse and several other factors, including: histories of trauma (in childhood, during military service) and discrimination, and associated mental health conditions; post-military socio-economic stressors; shifting social roles and adverse social support; and lost personal identity after military service. Psychosocial factors collectively underscore areas in which delivery of health and social services to women Veterans being treated in non-VA settings could be improved: (1) diffuse, implement, and sustain evidence-based gender-sensitive substance abuse treatment; (2) address traumas contributing to poor health; (3) recognize stress proliferation processes erode women's capacity to access healthcare or cope with stressors in healthy ways; (4) champion women Veterans who embody resilience and thereby can help others to form empowered personal identities of health and wellness.

CONCLUSION: Findings can inform interventions and services that ameliorate vulnerability to substance abuse and other health risks among women Veterans.

[Elevation of Hippocampal Neurogenesis Induces a Temporally Graded Pattern of Forgetting of Contextual Fear Memories.](#)

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J Neurosci. **2018 Mar 28**;38(13):3190-3198. doi: 10.1523/JNEUROSCI.3126-17.2018. PMID: 29453206. Epub 2018 Feb 16.

Throughout life neurons are continuously generated in the subgranular zone of the hippocampus. The subsequent integration of newly generated neurons alters patterns of dentate gyrus input and output connectivity, potentially rendering memories already stored in those circuits harder to access. Consistent with this prediction, we previously showed that increasing hippocampal neurogenesis after training induces forgetting of hippocampus-dependent memories, including contextual fear memory. However, the brain regions supporting contextual fear memories change with time, and this time-dependent memory reorganization might regulate the sensitivity of contextual fear memories to fluctuations in hippocampal neurogenesis. By virally expressing the inhibitory designer receptor exclusively activated by designer drugs, hM4Di, we first confirmed that chemogenetic inhibition of dorsal hippocampal neurons impairs retrieval of recent (day-old) but not remote (month-old) contextual fear memories in male mice. We then contrasted the effects of increasing hippocampal neurogenesis at recent versus remote time points after contextual fear conditioning in male and female mice. Increasing hippocampal neurogenesis immediately following training reduced conditioned freezing when mice were replaced in the context 1 month later. In contrast, when hippocampal neurogenesis was increased time points remote to training, conditioned freezing levels were unaltered when mice were subsequently tested. These temporally graded forgetting effects were observed using both environmental and genetic interventions to increase hippocampal neurogenesis. Our experiments identify memory age as a boundary condition for neurogenesis-mediated forgetting and suggest that, as contextual fear memories mature, they become less sensitive to changes in hippocampal neurogenesis levels because they no longer depend on the hippocampus for their expression.

SIGNIFICANCE STATEMENT: New neurons are generated in the hippocampus throughout life. As they integrate into the hippocampus, they remodel neural circuitry, potentially making information stored in those circuits harder to access. Consistent with this, increasing hippocampal neurogenesis after learning induces forgetting of the learnt information. The current study in mice asks whether these forgetting effects depend on the age of the memory. We found that post-training increases in hippocampal neurogenesis only impacted recently acquired, and not remotely acquired, hippocampal memories. These experiments identify memory age as a boundary condition for neurogenesis-mediated forgetting, and suggest remote memories are less sensitive to changes in hippocampal neurogenesis levels because they no longer depend critically on the hippocampus for their expression.

OTHER RESEARCH OF INTEREST (Continued)**[A Randomized Controlled Trial for Veterans with PTSD and Substance Use Disorder: Creating Change versus Seeking Safety.](#)**

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Subst Use Misuse. **2018 Sep 19**;53(11):1788-1800. doi: 10.1080/10826084.2018.1432653. PMID: 29461920. Epub 2018 Feb 20.

BACKGROUND: Posttraumatic stress disorder (PTSD) and substance use disorder (SUD) co-occur in military veterans and other populations.

OBJECTIVE: To conduct a randomized controlled trial to compare a new past-focused treatment (Creating Change; CC), to a well-established, evidence-based present-focused treatment for PTSD/SUD (Seeking Safety; SS), on symptoms of both disorders. CC guides patients to process the past through exploration of PTSD/SUD life themes and memories whereas SS focuses on coping skills in the present.

METHODS: Fifty-two male and female veterans with current PTSD/SUD were randomized (n = 26 per treatment) and assessed at baseline, end-of-treatment and 3-month follow-up. They received 17 individual one-hour sessions.

RESULTS: Intent-to-treat analyses indicated that both conditions improved over time, with no difference between conditions, on PTSD, alcohol use, and drug use (our primary outcomes) as well as mental health symptoms, quality of life, self-efficacy, and SUD cognitions. Effect sizes were medium except for alcohol use, which was large. Change over time reflected improvement from baseline to end-of-treatment, with gains sustained at follow-up, although alcohol use showed continued improvement from end-of-treatment to follow-up. Both treatments evidenced a strong safety profile; and attendance, alliance, and treatment satisfaction were also very strong. **Conclusions/importance:** CC has promise as a PTSD/SUD therapy with strong public health relevance and the potential to fill important gaps in the field. We used minimal exclusionary criteria to obtain a real-world sample, which was severe-predominantly substance-dependent with chronic PTSD and additional psychiatric diagnoses. Future research is warranted, especially on nonveteran samples and treatment mechanisms of action.

[The impact of exposure to air pollution on cognitive performance.](#)

[Zhang X](#)¹, [Chen X](#)^{2,3}, [Zhang X](#)^{4,5}.

Proc Natl Acad Sci U S A. **2018 Aug 27**. pii: 201809474. doi: 10.1073/pnas.1809474115. PMID: 30150383. [Epub ahead of print]

This paper examines the effect of both cumulative and transitory exposures to air pollution for the same individuals over time on cognitive performance by matching a nationally representative longitudinal survey and air quality data in China according to the exact time and geographic locations of the cognitive tests. We find that long-term exposure to air pollution impedes cognitive performance in verbal and math tests. We provide evidence that the effect of air pollution on verbal tests becomes more pronounced as people age, especially for men and the less educated. The damage on the aging brain by air pollution likely imposes substantial health and economic costs, considering that cognitive functioning is critical for the elderly for both running daily errands and making high-stake decisions.

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