

GULF WAR ILLNESS

[Reproducibility and validity of a novel invasive method of assessing peripheral microvascular vasomotor function.](#)

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PLoS One. 2019 Jan 25;14(1):e0211152. doi: 10.1371/journal.pone.0211152. PMID: 30682202. eCollection 2019.

In healthy arteries, blood flow is regulated by microvascular tone assessed by changes in blood flow volume and vascular resistance to endothelium-dependent and -independent vasodilators. We developed a novel method of using intravascular ultrasound (IVUS) and a Doppler flow wire to measure changes in blood flow volume and vascular resistance of the profunda arterial bed. We assessed the variability over 6 months in measuring microvascular endothelium-dependent dilation to acetylcholine and endothelium-independent dilation to adenosine in 20 subjects who were part of a larger study of Gulf War Illness without obstructive peripheral artery disease. Vasomotor function was assessed by Infusions of control (dextrose), acetylcholine (10-6M), adenosine (50µg), and nitroglycerin (25µg/ml). 400 IVUS and 240 flow velocity images were measured a mean 6 (SD = 2) months apart blind to measurement and infusion stage. The mean (SD) baseline profunda flow was 227 (172) ml/min and vascular resistance 4.6 x 10⁴ (2.4 x 10⁴) dynes-s/cm⁵. The intraclass correlation coefficients for 6-month variability for vascular function were excellent (range 0.827-0.995). Bland-Altman analyses showed mean differences of less than 2% for microvascular endothelium-dependent function (flow volume and resistance) and less than 1% for macrovascular endothelium-dependent function with acceptable limits of agreement. In 49 subjects assessing concurrent validity of the technique against atherosclerosis risk factors, we observed greater impairment in microvascular endothelium-dependent function per year of age (flow volume = -1.4% (p = 0.018), vascular resistance = 1.5% (p = 0.015)) and current smoking (flow volume = -36.7% (p = .006), vascular resistance = 50.0% (p<0.001)). This novel method of assessing microvascular vasomotor function had acceptable measurement reproducibility and validity.

CHRONIC FATIGUE SYNDROME

[Estimating Prevalence, Demographics, and Costs of ME/CFS Using Large Scale Medical Claims Data and Machine Learning.](#)

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Front Pediatr. 2019 Jan 8;6:412. doi: 10.3389/fped.2018.00412. PMID: 30671425. eCollection 2018.

Techniques of data mining and machine learning were applied to a large database of medical and facility claims from commercially insured patients to determine the prevalence, gender demographics, and costs for individuals with provider-assigned diagnosis codes for myalgic encephalomyelitis (ME) or chronic fatigue syndrome (CFS). The frequency of diagnosis was 519-1,038/100,000 with the relative risk of females being diagnosed with ME or CFS compared to males 1.238 and 1.178, respectively. While the percentage of women diagnosed with ME/CFS is higher than the percentage of men, ME/CFS is not a "women's disease." Thirty-five to forty percent of diagnosed patients are men. Extrapolating from this frequency of diagnosis and based on the estimated 2017 population of the United States, a rough estimate for the number of patients who may be diagnosed with ME or CFS in the U.S. is 1.7 million to 3.38 million. Patients diagnosed with CFS appear to represent a more heterogeneous group than those diagnosed with ME. A machine learning model based on characteristics of individuals diagnosed with ME was developed and applied, resulting in a predicted prevalence of 857/100,000 ($p > 0.01$), or roughly 2.8 million in the U.S. Average annual costs for individuals with a diagnosis of ME or CFS were compared with those for lupus (all categories) and multiple sclerosis (MS), and found to be 50% higher for ME and CFS than for lupus or MS, and three to four times higher than for the general insured population. A separate aspect of the study attempted to determine if a diagnosis of ME or CFS could be predicted based on symptom codes in the insurance claims records. Due to the absence of specific codes for some core symptoms, we were unable to validate that the information in insurance claims records is sufficient to identify diagnosed patients or suggest that a diagnosis of ME or CFS should be considered based solely on looking for presence of those symptoms. These results show that a prevalence rate of 857/100,000 for ME/CFS is not unreasonable; therefore, it is not a rare disease, but in fact a relatively common one.

CHRONIC FATIGUE SYNDROME (Continued)

[Relationship Between Exercise-induced Oxidative Stress Changes and Parasympathetic Activity in Chronic Fatigue Syndrome: An Observational Study and in Patients and Healthy Subjects.](#)

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Clin Ther. 2019 Jan 18. pii: S0149-2918(18)30611-8. doi: 10.1016/j.clinthera.2018.12.012. PMID: 30665828. [Epub ahead of print]

PURPOSE: Oxidative stress has been proposed as a contributor to pain in patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). During incremental exercise in patients with ME/CFS, oxidative stress enhances sooner and antioxidant response is delayed. We explored whether oxidative stress is associated with pain symptoms or pain changes following exercise, and the possible relationships between oxidative stress and parasympathetic vagal nerve activity in patients with ME/CFS versus healthy, inactive controls.

METHODS: The present study reports secondary outcomes from a previous work. Data from 36 participants were studied (women with ME/CFS and healthy controls). Subjects performed a submaximal exercise test with continuous cardiorespiratory monitoring. Levels of thiobarbituric acid-reactive substances (TBARSs) were used as a measure of oxidative stress, and heart rate variability was used to assess vagal activity. Before and after the exercise, subjects were asked to rate their pain using a visual analogic scale.

FINDINGS: Significant between-group differences in pain at both baseline and following exercise were found (both, $P < 0.007$). In healthy controls, pain was significantly improved following exercise ($P = 0.002$). No change in oxidative stress level after exercise was found. Significant correlation between TBARS levels and pain was found at baseline ($r = 0.540$; $P = 0.021$) and after exercise ($r = 0.524$; $P = 0.024$) in patients only. No significant correlation between TBARS and heart rate variability at baseline or following exercise was found in either group. However, a significant correlation was found between exercise-induced changes in HRV and TBARS in healthy controls ($r = -0.720$; $P = 0.001$).

IMPLICATIONS: Oxidative stress showed an association with pain symptoms in people with ME/CFS, but no exercise-induced changes in oxidative stress were found. In addition, the change in parasympathetic activity following exercise partially accounted for the change in oxidative stress in healthy controls. More research is required to further explore this link.

[Chronic fatigue syndrome in the emergency department.](#)

[Timbol CR](#)¹, [Baraniuk JN](#)¹.

Open Access Emerg Med. 2019 Jan 11;11:15-28. doi: 10.2147/OAEM.S176843. PMID: 30666170. eCollection 2019.

Purpose: Chronic fatigue syndrome (CFS) is a debilitating disease characterized by fatigue, postexertional malaise, cognitive dysfunction, sleep disturbances, and widespread pain. A pilot, online survey was used to determine the common presentations of CFS patients in the emergency department (ED) and attitudes about their encounters.

Methods: The anonymous survey was created to score the severity of core CFS symptoms, reasons for going to the ED, and Likert scales to grade attitudes and impressions of care. Open text fields were qualitatively categorized to determine common themes about encounters.

Results: Fifty-nine percent of respondents with physician-diagnosed CFS (total $n=282$) had gone to an ED. One-third of ED presentations were consistent with orthostatic intolerance; 42% of participants were dismissed as having psychosomatic complaints. ED staff were not knowledgeable about CFS. Encounters were unfavorable (3.6 on 10-point scale). The remaining 41% of subjects did not go to ED, stating nothing could be done or they would not be taken seriously. CFS subjects can be identified by a CFS questionnaire and the prolonged presence (>6 months) of unremitting fatigue, cognitive, sleep, and postexertional malaise problems.

Conclusion: This is the first investigation of the presentation of CFS in the ED and indicates the importance of orthostatic intolerance as the most frequent acute cause for a visit. The self-report CFS questionnaire may be useful as a screening instrument in the ED. Education of ED staff about modern concepts of CFS is necessary to improve patient and staff satisfaction. Guidance is provided for the diagnosis and treatment of CFS in these challenging encounters.

HEADACHE and MIGRAINE

Device for Cluster Headache.

[Voelker R.](#)

JAMA. 2019 Jan 22;321(3):239. doi: 10.1001/jama.2018.21464. PMID: 30667491.

News From the Food and Drug Administration

The FDA has [cleared](#) a noninvasive vagus nerve stimulator as the first device indicated to help prevent cluster headaches in adults.

Initially [approved](#) in 2017 to treat acute pain from episodic cluster headache, gammaCore also was cleared last year as an acute treatment for adults with migraine pain. Patients can place the handheld device against their neck over the vagus nerve to deliver mild electrical stimulation. To prevent cluster headaches, patients use gammaCore twice a day in 3 consecutive 2-minute stimulations. The first treatment should be within an hour of waking and the second 7 to 10 hours later.

Experiences of an outpatient infusion center with intravenous magnesium therapy for status migrainosus.

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Clin Neurol Neurosurg. 2019 Jan 21;178:31-35. doi: 10.1016/j.clineuro.2019.01.007. PMID: 30685601. [Epub ahead of print]

OBJECTIVES: Exploratory study to investigate the effectiveness of intravenous magnesium as an abortive for status migrainosus in an outpatient infusion center, and characterize the patients who benefit from the therapy.

PATIENTS & METHODS: Retrospective analysis of 234 migraine patients who received IV magnesium as a headache abortive, at the headache clinic of University of Southern California. Additional intramuscular (IM) injections for nausea (prochlorperazine, ondansetron, metoclopramide) or for refractory pain (ketorolac, dexamethasone, sumatriptan, dihydroergotamine), were administered as necessary. Immediately before and after treatment, self-reported pain levels were recorded using an 11-point numeric pain rating scale (0-10).

RESULTS: Our patient sample has a mean age of 44 years and was predominantly female (79%). 36 (19%) had migraine with aura. Overall, pain score decreased from 5.46 ± 2.39 to 3.56 ± 2.75 ($P < 0.001$) after magnesium infusion. One hundred twenty-seven (54%) patients had clinically significant pain reduction, as defined by pain decrease $\geq 30\%$. One hundred and four patients (44%) received IV magnesium and did not require additional intramuscular (IM) medications for pain. In patients who did not receive additional IM medications for pain, pain score decreased from 4.76 ± 2.41 to 2.95 ± 2.70 ($p < 0.001$), and 61 out of 104 (59%) experienced $\geq 30\%$ pain reduction. Patients with less severe pain tended to have a better response than patients with more severe pain, as patients with $\geq 30\%$ pain reduction had a significantly lower pre-treatment pain score ($p = 0.018$).

CONCLUSION: For a subset of patients with status migrainosus, IV magnesium therapy results in clinically significant pain relief without the need for intramuscular pain medications. Therefore, IV magnesium may be useful as a cost-effective first-line parental therapy for status migrainosus, especially for patients who initially present with lower pain intensity.

HEADACHE and MIGRAINE (Continued)

[Association Between Migraine and Benign Paroxysmal Positional Vertigo Among Adults in South Korea.](#)

[Kim SK](#)¹, [Hong SM](#)¹, [Park IS](#)¹, [Choi HG](#)².

JAMA Otolaryngol Head Neck Surg. 2019 Jan 24. doi: 10.1001/jamaoto.2018.4016. PMID: 30676633. [Epub ahead of print]

Importance: Patients with migraine often experience various types of vertigo, and several studies have suggested an epidemiologic and physiologic association of migraine and vertigo with vestibule. However, few researchers have investigated the association between migraine and benign paroxysmal positional vertigo (BPPV).

Objective: To determine the incidence of BPPV in individuals with migraine in a large national population-based sample.

Design, Setting, and Participants: This cohort study obtained data from the Korean Health Insurance Review and Assessment Service covering the period January 1, 2002, through December 31, 2013. These data included personal information, health insurance claim codes, diagnostic codes, death records, socioeconomic data, and medical examination data for each individual in the database. A 1:4 matching method was used to select individuals for the migraine group (n = 40 682) and the control group (n = 162 728). Individuals who had a history of BPPV before the index date, for whom a match could not be identified, and who received a migraine diagnosis before age 20 years were excluded from the analysis. Data analysis was conducted from September 1, 2015, to December 31, 2017.

Main Outcomes and Measures: The crude and adjusted (by age, sex, income, region of residence, and medical history [hypertension, diabetes, or dyslipidemia]) hazard ratios for migraine and BPPV were analyzed using the Cox proportional hazards regression model.

Results: Of the 40 682 individuals in the migraine group, 10 381 (25.5%) were male and 30 301 (74.5%) were female. Of the 162 728 controls, 41 524 (25.5%) were male and 121 204 (74.5%) were female. The incidence of BPPV was statistically significantly higher in the migraine group than in the control group (2431 [6.0%] vs 3677 [2.3%]). Migraine increased the risk of BPPV (adjusted hazard ratio, 2.54; 95% CI, 2.41-2.68). In a subgroup analysis, the incidence of BPPV in all age groups and in both men and women was statistically significantly higher in the migraine group than in the control group. The incidence of BPPV was the highest in men younger than 40 years (adjusted hazard ratio, 4.49; 95% CI, 3.05-6.62), and the HR decreased in both men and women as age increased.

Conclusions and Relevance: Migraine appeared to be statistically significantly associated with higher incidence of BPPV; future studies are needed to determine the association between BPPV and specific factors related to migraine.

[Impact of chronic headache on workdays, unemployment and disutility in the general population.](#)

[Kristoffersen ES](#)^{1,2,3}, [Stavem K](#)^{4,5,6}, [Lundqvist C](#)^{1,4,6,3}, [Russell MB](#)^{1,4}.

J Epidemiol Community Health. 2019 Jan 25. pii: jech-2018-211127. doi: 10.1136/jech-2018-211127. PMID: 30683804. [Epub ahead of print]

BACKGROUND: Data on the socioeconomic burden of chronic headache (≥ 15 days/last month or > 180 days/year) is lacking. This study investigated the impact of chronic headache on sickness absence, unemployment and disutility in the general population in Norway.

METHODS: 30 000 persons aged 30-44 from the general population were screened for chronic headache by a screening questionnaire. The responder rate was 71%. The International Classification of Headache Disorders was used. We analysed the association of chronic headache with lost workdays, days with $\geq 50\%$ reduced productivity, sick leave, unemployment and disutility, as assessed with the Short-Form Six-Dimension (SF-6D) in separate regression analyses.

RESULTS: Eighty-three per cent (427/516, 79% women) of the eligible participants completed the data on workdays and utility. They reported a mean of 9.7 (SD 24.8) workdays lost over the last 3 months, because of headache. The mean disutility score (1-SF-6D score) was 0.41. Thirty-three per cent were on long-term (> 1 year) sick leave. The OR for being on sick leave was 1.9 (95% CI 1.1 to 3.2, $p=0.017$) for those with secondary compared with primary chronic headache. Similarly, the OR for increased number of workdays lost to headache was 3.5 (95% CI 1.8 to 6.5, $p<0.001$) and for unemployment 1.7 (95% CI 1.0 to 2.9, $p=0.07$), for those with secondary compared with primary chronic headache. Secondary chronic headache, high headache frequency and high psychological distress were significantly associated with higher disutility score.

CONCLUSIONS: The burden of chronic headache in the general population is substantial with high rates of lost workdays and disutility.

CHRONIC PAIN

[Do patient perceptions of provider communication relate to experiences of physical pain?](#)

[Ruben MA](#)¹, [Meterko M](#)², [Bokhour BG](#)³.

Patient Educ Couns. **2018 Feb**;101(2):209-213. doi: 10.1016/j.pec.2017.08.002. PMID: 28803029. Epub 2017 Aug 4.

[Delayed PubMed posting of *Patient Education and Counseling* 2018 Article.]

OBJECTIVES: Patient-provider communication is an important component of the medical interaction yet little research has examined the relationships between perceptions of communication and health outcomes or the mechanisms by which communication may ameliorate the pain experience. This is the first study to examine the relationships between patients' perceptions of provider communication, pain intensity and self-efficacy for managing chronic disease.

METHODS: The total sample contained 1027 (85.8% male) Veteran patients. Patients responded to surveys about their experiences and outcomes of care, including measures of patient-provider communication, self-efficacy and pain outcomes including pain intensity and pain interference.

RESULTS: Results showed more positive perceptions of provider communication were related to lower levels of pain intensity and pain interference and that this relationship was significantly mediated by higher levels of self-efficacy for managing chronic disease.

CONCLUSION: More positive provider communication was related to higher levels of self-efficacy, which in turn was related to lower levels of pain intensity and pain interference. Findings suggest that providers may be able to elicit higher levels of self-efficacy in their patients by providing patient-centered communication, which in turn will reduce pain intensity and interference in their patient's lives.

[CYP2D6-guided opioid therapy improves pain control in CYP2D6 intermediate and poor metabolizers: a pragmatic clinical trial.](#)

[Smith DM](#)¹, [Weitzel KW](#)^{1,2}, [Elsei AR](#)^{1,3}, [Langaee T](#)^{1,2}, [Gong Y](#)^{1,2}, [Wake DT](#)¹, [Duong BQ](#)¹, [Hagen M](#)⁴, [Harle CA](#)⁵, [Mercado E](#)⁶, [Nagoshi Y](#)⁴, [Newsom K](#)⁷, [Wright A](#)⁴, [Rosenberg E](#)⁴, [Starostik P](#)^{7,8}, [Clare-Salzler MJ](#)⁷, [Schmidt SO](#)⁶, [Fillingim RB](#)^{3,9}, [Johnson JA](#)^{1,2,3}, [Cavallari LH](#)^{10,11,12}.

Genet Med. **2019 Jan 23**. doi: 10.1038/s41436-018-0431-8. PMID: 30670877. [Epub ahead of print]

PURPOSE: CYP2D6 bioactivates codeine and tramadol, with intermediate and poor metabolizers (IMs and PMs) expected to have impaired analgesia. This pragmatic proof-of-concept trial tested the effects of CYP2D6-guided opioid prescribing on pain control.

METHODS: Participants with chronic pain (94% on an opioid) from seven clinics were enrolled into CYP2D6-guided (n = 235) or usual care (n = 135) arms using a cluster design. CYP2D6 phenotypes were assigned based on genotype and CYP2D6 inhibitor use, with recommendations for opioid prescribing made in the CYP2D6-guided arm. Pain was assessed at baseline and 3 months using PROMIS® measures.

RESULTS: On stepwise multiple linear regression, the primary outcome of composite pain intensity (composite of current pain and worst and average pain in the past week) among IM/PMs initially prescribed tramadol/codeine (n = 45) had greater improvement in the CYP2D6-guided versus usual care arm (-1.01 ± 1.59 vs. -0.40 ± 1.20 ; adj P = 0.016); 24% of CYP2D6-guided versus 0% of usual care participants reported $\geq 30\%$ (clinically meaningful) reduction in the composite outcome. In contrast, among normal metabolizers prescribed tramadol or codeine at baseline, there was no difference in the change in composite pain intensity at 3 months between CYP2D6-guided (-0.61 ± 1.39) and usual care (-0.54 ± 1.69) groups (adj P = 0.540).

CONCLUSION: These data support the potential benefits of CYP2D6-guided pain management.

OTHER RESEARCH OF INTEREST

[Trust in Health Care.](#)

[Bauchner H](#)¹.

JAMA. 2019 Jan 24. doi: 10.1001/jama.2018.20795. PMID: 30676627 [Epub ahead of print]

[Link to [JAMA Editorial](#)]

Trust is defined by the *Merriam-Webster* dictionary as “assured reliance on the character, ability, strength, or truth of someone or something.” The Oxford dictionary has a similar definition: “firm belief in the reliability, truth, or ability of someone or something.”

In this issue of *JAMA* is the initial Viewpoint of a series that will focus on important aspects of trust in health care. Because of the heightened rhetoric in politics in the United States and around the world, concerns that social media may be blurring the distinction between truth and fiction, increasing concerns about conflict of interest and scientific misconduct in medicine, and the general upheaval in health care, trust in the various institutions that comprise the US health care enterprise has emerged as an important issue.

Because of these concerns, the American Board of Internal Medicine Foundation focused on trust in health care at its annual retreat in 2018. Participants were assembled in small groups and over 2 days discussed the importance of trust in the various institutions that comprise the US health care system. A series of Viewpoints emerged from this meeting.

The first Viewpoint, by Lee and coauthors, focuses on trust between patients and the organizations and physicians that care for them—the fundamental building block of the patient-physician relationship. In this Viewpoint the authors explore the problem of trust in the health care system and propose a series of recommendations that they believe will enhance trust.

After the series concludes, an Editorial will reflect on the various Viewpoints and explore the importance of trust in health care.

[A Framework for Increasing Trust Between Patients and the Organizations That Care for Them.](#)

[Lee TH](#)¹, [McGlynn EA](#)², [Safran DG](#)³.

JAMA. 2019 Jan 24. doi: 10.1001/jama.2018.19186. PMID: 30676628. [Epub ahead of print]

[Link to full text of [JAMA Viewpoint Article](#)]

Trust matters in health care. It makes patients feel less vulnerable, clinicians feel more effective, and reduces the imbalances of information by improving the flow of information. Trust is so fundamental to the patient-physician relationship that it is easy to assume it exists. But because of changes in health care and society at large, trust is increasingly understood to be at risk and in need of attention.

The Problem: Trust is at risk because the US health care system has evolved in ways that (whether intentional or not) are deprioritizing relationships. Today, trust must be based on more than patient-physician relationships because much of the state-of-the-science care requires groups of clinicians to work in teams, and patients must trust the overall team as well as its individual members.

Cultivating the trust of patients in the teams delivering their care would be simpler if those teams were well established, but many teams do not function well. Clinicians caring for a patient may not know or talk to each other, and all too often may just focus on the narrow areas of their expertise. However, there are exceptions such as multidisciplinary integrated practice units that are organized around patient conditions and take responsibility for patients across the continuum of care (eg, heart failure teams) and well-run and efficient ambulatory practices that do function as a team. The regularity of interactions among personnel and between the clinician and the patient provides the opportunity for the building of trust. Integrated practice units are becoming more common at larger medical centers, but still deliver only a small percentage of care.

Most clinicians have not cultivated the ability to form effective teams among personnel who may not have met before. However, examples of effective teams can be found on a daily basis in operating rooms where the use of the surgical checklist helps ensure that everyone introduces himself or herself and has the same understanding of the procedure to be undertaken. Even though many surgeons and other operating personnel were resistant to expectations that they use the surgical checklist when it was introduced, 93.4% (of 257 clinicians surveyed) indicated that if they were having a procedure performed on them, they would want the checklist used. That insight helped operating room personnel understand that the checklist had cultural goals beyond the obvious immediate focus on safety issues. The checklist helped build the team’s sense of shared purpose, and when clinicians imagined themselves as patients, they understood that such cohesiveness enhanced trust.

OTHER RESEARCH OF INTEREST (Continued)

Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia: A Randomized Clinical Trial.

[SPRINT MIND Investigators for the SPRINT Research Group](#), [Williamson JD¹](#), [Pajewski NM²](#), [Auchus AP³](#), [Bryan RN⁴](#), [Chelune G⁵](#), [Cheung AK⁶](#), [Cleveland ML¹](#), [Coker LH⁷](#), [Crowe MG⁸](#), [Cushman WC⁹](#), [Cutler JA¹⁰](#), [Davatzikos C⁴](#), [Desiderio L⁴](#), [Erus G⁴](#), [Fine LJ¹¹](#), [Gaussoin SA²](#), [Harris D²](#), [Hsieh MK⁴](#), [Johnson KC¹²](#), [Kimmel PL¹³](#), [Tamura MK¹⁴](#), [Launer LJ¹⁵](#), [Lerner AJ¹⁶](#), [Lewis CE¹⁷](#), [Martindale-Adams J¹²](#), [Moy CS¹⁸](#), [Nasrallah IM⁴](#), [Nichols LO⁹](#), [Oparil S¹⁹](#), [Ogrocki PK¹⁶](#), [Rahman M²⁰](#), [Rapp SR²¹](#), [Reboussin DM²](#), [Rocco MV²²](#), [Sachs BC²³](#), [Sink KM¹](#), [Still CH²⁴](#), [Supiano MA²⁵](#), [Snyder JK¹⁰](#), [Wadley VG¹⁹](#), [Walker J¹](#), [Weiner DE²⁶](#), [Whelton PK²⁷](#), [Wilson VM¹](#), [Woolard N¹](#), [Wright JT Jr²⁸](#), [Wright CB¹⁸](#).

JAMA. 2019 Jan 28. doi: 10.1001/jama.2018.21442. PMID: 30688979. [Epub ahead of print]

Importance: There are currently no proven treatments to reduce the risk of mild cognitive impairment and dementia.

Objective: To evaluate the effect of intensive blood pressure control on risk of dementia.

Design, Setting, and Participants: Randomized clinical trial conducted at 102 sites in the United States and Puerto Rico among adults aged 50 years or older with hypertension but without diabetes or history of stroke. Randomization began on November 8, 2010. The trial was stopped early for benefit on its primary outcome (a composite of cardiovascular events) and all-cause mortality on August 20, 2015. The final date for follow-up of cognitive outcomes was July 22, 2018.

Interventions: Participants were randomized to a systolic blood pressure goal of either less than 120 mm Hg (intensive treatment group; n = 4678) or less than 140 mm Hg (standard treatment group; n = 4683).

Main Outcomes and Measures: The primary cognitive outcome was occurrence of adjudicated probable dementia. Secondary cognitive outcomes included adjudicated mild cognitive impairment and a composite outcome of mild cognitive impairment or probable dementia.

Results: Among 9361 randomized participants (mean age, 67.9 years; 3332 women [35.6%]), 8563 (91.5%) completed at least 1 follow-up cognitive assessment. The median intervention period was 3.34 years. During a total median follow-up of 5.11 years, adjudicated probable dementia occurred in 149 participants in the intensive treatment group vs 176 in the standard treatment group (7.2 vs 8.6 cases per 1000 person-years; hazard ratio [HR], 0.83; 95% CI, 0.67-1.04). Intensive BP control significantly reduced the risk of mild cognitive impairment (14.6 vs 18.3 cases per 1000 person-years; HR, 0.81; 95% CI, 0.69-0.95) and the combined rate of mild cognitive impairment or probable dementia (20.2 vs 24.1 cases per 1000 person-years; HR, 0.85; 95% CI, 0.74-0.97).

Conclusions and Relevance: Among ambulatory adults with hypertension, treating to a systolic blood pressure goal of less than 120 mm Hg compared with a goal of less than 140 mm Hg did not result in a significant reduction in the risk of probable dementia. Because of early study termination and fewer than expected cases of dementia, the study may have been underpowered for this end point.

Trial Registration: ClinicalTrials.gov Identifier: [NCT01206062](#).

Effect of Sedentary Lifestyle on Cardiovascular Disease Risk Among Healthy Adults With Body Mass Indexes 18.5 to 29.9 kg/m².

[Mainous AG 3rd¹](#), [Tanner RJ²](#), [Rahmanian KP³](#), [Jo A²](#), [Carek PJ⁴](#).

Am J Cardiol. 2018 Dec 4. pii: S0002-9149(18)32148-9. doi: 10.1016/j.amjcard.2018.11.043. PMID: 30554650. [Epub ahead of print]

A substantial proportion of adults at healthy body mass index (BMI) are potentially at high risk for cardiovascular disease (CVD). The objective of this study is to determine if sedentary lifestyle characteristics in healthy weight adults increase their likelihood of being at high CVD risk to that of individuals who are overweight. Adults aged 40 to 79 years in the 2011 to 2016 National Health and Nutrition Examination Survey at a healthy BMI (18.5 to 24.9) and overweight BMI (25 to 29.9; unweighted n = 4,572; weighted n = 43,919,354) were analyzed. The American College of Cardiology/American Heart Association atherosclerotic CVD risk score was used to assess CVD risk. For individuals with a BMI 18.5 to 24.9, 29.6% had increased risk of a CVD event. In logistic regressions adjusted for age, race, gender, education, poverty/income ratio, insurance status, and number of visits to a healthcare provider in the past year, individuals with unhealthy sagittal abdominal diameter (odds ratio [OR] 2.44; 95% confidence interval [CI], 0.97 to 6.14), shortness of breath upon exertion (OR 1.35; 95% CI, 0.65 to 2.79), unhealthy waist circumference (OR 0.99; 95% CI, 0.60 to 1.61), and less than recommended levels of physical activity (OR 0.73; 95% CI, 0.43 to 1.23) were not significantly different than overweight adults in being at high risk for CVD events. Individuals with healthy characteristics and a BMI 18.5 to 24.9 were significantly less likely than overweight adults to be at high risk for CVD. In conclusion, the findings suggest that in individuals at a BMI 18.5 to 24.9, characteristics of a sedentary lifestyle increase the likelihood of being at high risk for CVD to that of overweight individuals.

OTHER RESEARCH OF INTEREST (Continued)**[Insomnia disorder subtypes derived from life history and traits of affect and personality.](#)**

[Blanken TF](#)¹, [Benjamins JS](#)², [Borsboom D](#)³, [Vermunt JK](#)⁴, [Paquola C](#)⁵, [Ramautar J](#)⁶, [Dekker K](#)⁶, [Stoffers D](#)⁷, [Wassing R](#)⁶, [Wei Y](#)⁶, [Van Someren EJW](#)⁸.

Lancet Psychiatry. 2019 Jan 7. pii: S2215-0366(18)30464-4. doi: 10.1016/S2215-0366(18)30464-4. PMID: 30630691. [Epub ahead of print]

BACKGROUND: Insomnia disorder is the second most prevalent mental disorder, and it is a primary risk factor for depression. Inconsistent clinical and biomarker findings in patients with insomnia disorder suggest that heterogeneity exists and that subtypes of this disease remain unrecognised. Previous top-down proposed subtypes in nosologies have had insufficient validity. In this large-scale study, we aimed to reveal robust subtypes of insomnia disorder by use of data-driven analyses on a multidimensional set of biologically based traits.

METHODS: In this series of studies, we recruited participants from the Netherlands Sleep Registry, a database of volunteers aged 18 years or older, who we followed up online to survey traits, sleep, life events, and health history with 34 selected questionnaires of which participants completed at least one. We identified insomnia disorder subtypes by use of latent class analyses. We evaluated the value of our identified subtypes of insomnia disorder by use of a second, non-overlapping cohort who were recruited through a newsletter that was emailed to a new sample of Netherlands Sleep Registry participants, and by assessment of within-subject stability over several years of follow-up. We extensively tested the clinical validity of these subtypes for the development of sleep complaints, comorbidities (including depression), and response to benzodiazepines; in two subtypes of insomnia disorder, we also assessed the clinical relevance of these subtypes by use of an electroencephalogram biomarker and the effectiveness of cognitive behavioural therapy. To facilitate implementation, we subsequently constructed a concise subtype questionnaire and we validated this questionnaire in the second, non-overlapping cohort.

FINDINGS: 4322 Netherlands Sleep Registry participants completed at least one of the selected questionnaires, a demographic questionnaire, and an assessment of their Insomnia Severity Index (ISI) between March 2, 2010, and Oct 28, 2016. 2224 (51%) participants had probable insomnia disorder, defined as an ISI score of at least 10, and 2098 (49%) participants with a lower ISI score served as a control group. With a latent class analysis of the questionnaire responses of 2224 participants, we identified five novel insomnia disorder subtypes: highly distressed, moderately distressed but reward sensitive (ie, with intact responses to pleasurable emotions), moderately distressed and reward insensitive, slightly distressed with high reactivity (to their environment and life events), and slightly distressed with low reactivity. In a second, non-overlapping replication sample of 251 new participants who were assessed between June 12, 2017, and Nov 26, 2017, five subtypes were also identified to be optimal. In both the development sample and replication sample, each participant was classified as having only one subtype with high posterior probability (0.91-1.00). In 215 of the original sample of 2224 participants with insomnia who were reassessed 4.8 (SD 1.6) years later (between April 13, 2017, and June 21, 2017), the probability of maintaining their original subtype was 0.87, indicating a high stability of the classification. We found differences between the identified subtypes in developmental trajectories, response to treatment, the presence of an electroencephalogram biomarker, and the risk of depression that was up to five times different between groups, which indicated a clinical relevance of these subtypes.

INTERPRETATION: High-dimensional data-driven subtyping of people with insomnia has addressed an unmet need to reduce the heterogeneity of insomnia disorder. Subtyping facilitates identification of the underlying causes of insomnia, development of personalised treatments, and selection of patients with the highest risk of depression for inclusion in trials regarding prevention of depression.

FUNDING: European Research Council and Netherlands Organization for Scientific Research.

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