

## 7. PELVIC ORGANS/WOMAN'S HEALTH

### Breast CA risk

#### **Breast Cancer Risk After Recent Childbirth: A Pooled Analysis of 15 Prospective Studies**

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**Background:** Parity is widely recognized as protective for breast cancer, but breast cancer risk may be increased shortly after childbirth. Whether this risk varies with breastfeeding, family history of breast cancer, or specific tumor subtype has rarely been evaluated.

**Objective:** To characterize breast cancer risk in relation to recent childbirth.

**Design:** Pooled analysis of individual-level data from 15 prospective cohort studies.

**Setting:** The international Premenopausal Breast Cancer Collaborative Group.

**Participants:** Women younger than 55 years.

**Measurements:** During 9.6 million person-years of follow-up, 18 826 incident cases of breast cancer were diagnosed. Hazard ratios (HRs) and 95% CIs for breast cancer were calculated using Cox proportional hazards regression.

**Results:** Compared with nulliparous women, parous women had an HR for breast cancer that peaked about 5 years after birth (HR, 1.80 [95% CI, 1.63 to 1.99]) before decreasing to 0.77 (CI, 0.67 to 0.88) after 34 years. The association crossed over from positive to negative about 24 years after birth. The overall pattern was driven by estrogen receptor (ER)-positive breast cancer; no crossover was seen for ER-negative cancer. Increases in breast cancer risk after childbirth were pronounced when combined with a family history of breast cancer and were greater for women who were older at first birth or who had more births. Breastfeeding did not modify overall risk patterns.

**Limitations:** Breast cancer diagnoses during pregnancy were not uniformly distinguishable from early postpartum diagnoses. Data on human epidermal growth factor receptor 2 (*HER2*) oncogene overexpression were limited.

**Conclusion:** Compared with nulliparous women, parous women have an increased risk for breast cancer for more than 20 years after childbirth. Health care providers should consider recent childbirth a risk factor for breast cancer in young women.

## 8. VISCERA

### Association of hypertension and cognitive function

J Clin Hypertens (Greenwich). 2018 Nov;20(11):1575-1583. doi: 10.1111/jch.13393. Epub 2018 Sep 26.

#### **Association between hypertension and cognitive function: A cross-sectional study in people over 45 years old in China.**

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This cross-sectional study aimed to evaluate the associations of characteristics of hypertension, including hypertension status, duration, blood pressure (BP), and pulse pressure (PP), with two cognitive functions-episodic memory and executive function, in people aged over 45 years.

Using 2013 survey of the China Health and Retirement Longitudinal Study (CHARLS) and weighted multiple linear regression, data from 6,732 participants were utilized. After fully adjusted in full sample, a significantly ( $P < 0.05$ ) negative association was found between treated but uncontrolled hypertension and cognition. In people aged 45-59 years, there was no significant association between hypertension and cognition. However, in people aged  $\geq 60$  years, the systolic blood pressure (SBP) and PP showed significantly adverse correlations to cognition.

The negative association of untreated, treated but uncontrolled hypertension, and elevated PP with cognition increased with aging. In conclusion, this study shows the correlation between hypertension and cognition was age-dependent with greater correlation in older people; uncontrolled hypertension and PP may be used as predictors of the cognitive decline in people  $\geq 75$  years.

## Autism and neurotransmitters

### Association of autism spectrum disorder with prenatal exposure to medication affecting neurotransmitter systems

JAMA —

Janecka M, et al. | December 07, 2018

The physicians studied the connection of early-life interference with various neurotransmitter systems by prenatal medication exposure on the risk of autism spectrum disorder (ASD) in children. In this research, it was concluded that most of the medications which affected the neurotransmitter systems were found in no relation with the assessments of ASD risk. It was also found that replication and/or validation using experimental techniques were also needed.

#### Methods

- In this case-control study, the investigators included the children who were born between January 1, 1997 and December 31, 2007, and were followed up for ASD till January 26, 2015, in a single health maintenance organization of Israel.
- In this sample, pregnant women who were given 55 groups of medications which could affect neurotransmitter systems were identified by using publicly available data.
- Children who were prenatally exposed to medications were then compared with those of nonexposed.
- They analyzed the data from March 1, 2017, through June 20, 2018.
- Main outcome and measures included hazard ratios (HRs) and 95% CIs of ASD risk were found linked to exposed medication groups using Cox proportional hazards regression, adjusted for the associated confounders (eg, birth year, maternal age, maternal history of psychiatric and neurologic disorders, or maternal number of all medical diagnoses 1 year before pregnancy).

#### Results

- A sum of 96,249 individuals (1,405 cases; 94,844 controls; mean [SD] age at the end of follow-up, 11.6 [3.1] years; 48.8% female), including 1,405 with ASD and 94,844 controls were involved in this study.
- Five out of 34 groups of medications showed minute statistically significant relations with ASD in fully adjusted models.
- Proof of confounding impacts of the number of maternal diagnoses on the association between children exposure to medication and ASD was found.
- After adjusting for this factor, the lower calculations of ASD risk among children exposed to cannabinoid receptor agonists (HR, 0.72; 95% CI, 0.55-0.95;  $P=.02$ ), muscarinic receptor 2 agonists (HR, 0.49; 95% CI, 0.24-0.98;  $P=.04$ ), opioid receptor  $\kappa$  and  $\epsilon$  agonists (HR, 0.67; 95% CI, 0.45-0.99;  $P=.045$ ), or  $\alpha_{2C}$ -adrenergic receptor agonists (HR, 0.43; 95% CI, 0.19-0.96;  $P=.04$ ) were recognized.
- It was also observed that exposure to antagonists of neuronal nicotinic acetylcholine receptor  $\alpha$  was linked to higher estimates of ASD risk (HR, 12.94; 95% CI, 1.35-124.25;  $P=.03$ ).

**Psoriasis and IBS****Association of psoriasis with inflammatory bowel disease: A systematic review and meta-analysis**

JAMA — Fu Y, et al. | December 14, 2018

In order to investigate the association of psoriasis with inflammatory bowel disease (IBD), researchers carried out a systematic review and meta-analysis. Findings suggested a significant association of psoriasis with IBD. When patients with psoriasis present with bowel symptoms, a gastroenterology consultation is suggested.

## Methods

- MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials were searched for relevant studies from the start to January 17, 2018 for this investigation.
- Researchers included the case-control, cross-sectional, or cohort studies that examined either the odds or risk of IBD in patients with psoriasis.
- In the search, no geographic or language limitations were used.
- The PRISMA and MOOSE guidelines for data extraction were followed.
- In order to assess the risk of bias of included studies, the Newcastle-Ottawa Scale was used.
- They separately analyzed Crohn disease and ulcerative colitis and conducted random-effects model meta-analysis.
- They performed a subgroup analysis on psoriatic arthritis.
- Main outcomes and measures included the risk and odds of IBD, Crohn disease, and ulcerative colitis in patients with psoriasis.

## Results

- There were a total of 5 case-control or cross-sectional studies and 4 cohort studies with 7,794,087 study participants.
- Psoriasis and Crohn disease (odds ratio, 1.70; 95% CI, 1.20-2.40) and psoriasis and ulcerative colitis (odds ratio, 1.75; 95% CI, 1.49-2.05) were significantly associated.
- The risk of Crohn disease (risk ratio, 2.53; 95% CI, 1.65-3.89) and ulcerative colitis (risk ratio, 1.71; 95% CI, 1.55-1.89) was increased in patients with psoriasis.

### Pediatric IBS

#### **Biochemical markers, genotype, and inflammation in pediatric inflammatory bowel disease: A Danish population-based study**

Digestive Diseases

Ziade F, et al. | December 13, 2018

Researchers involved 190 inflammatory bowel disease (IBD) subjects (ie, 97 ulcerative colitis [UC], 87 Crohn's disease [CD] and 6 IBD unclassified) from Eastern Denmark and selected 52 single nucleotide polymorphisms (SNPs) known to be linked to IBD, to identify and evaluate the efficacy of biochemical markers at diagnosis, to prognosticate disease course and also to examine the effects of genotype on biochemical markers of inflammation.

They observed a higher C-reactive protein, erythrocyte sedimentation rate, and platelet count at diagnosis in extensive UC sufferers but no changes in CD cases. They also found a low albumin level with an increased risk of surgery in both UC and CD subjects and increased use of azathioprine and anti-tumor necrosis factor alpha use.

The patient's genotype likely to affect the inflammatory response as one SNP (rs4986791 in the TLR-4 locus) and 2 SNPs (rs6785049 in the Pregnane-x-receptor gene and rs10500264 in the SLCA10 gene) were observed correlated with a change in albumin and hemoglobin and verifying that albumin might be a marker of severe disease course.

**PPI's increases risk of hip fx**

Osteoporosis International pp 1–12|

**Proton pump inhibitors and risk of hip fracture: a meta-analysis of observational studies**

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**Summary**

We performed a meta-analysis of relevant studies to quantify the magnitude of the association between proton pump inhibitors (PPIs) and risk of hip fracture. Patients with PPIs had a greater risk of hip fracture than those without PPI therapy (RR 1.20, 95% CI 1.14–1.28,  $p < 0.0001$ ). These results could be taken into consideration with caution, and patients should also be concerned about the inappropriate use of PPIs.

**Introduction** Proton pump inhibitors (PPIs) are generally considered as first-line medicine with great safety profile, commonly prescribed for gastroesophageal reflux disease (GERD) and peptic ulcer disease. However, several epidemiological studies documented that long-term use of PPIs may be associated with an increased risk of hip fracture. Although, the optimal magnitude of the hip fracture risk is still undetermined. We, therefore, performed a meta-analysis of relevant studies to quantify the magnitude of the association between PPIs and risk of hip fracture.

**Methods**

We collected relevant articles using MEDLINE, EMBASE, Google Scholar, and Web of Science from January 1, 1990, to March 31, 2018. We included only the large ( $n \geq 500$ ) observational studies with a follow-up duration of at least one year in which the hip fracture patients were identified by a standard procedure. Two of the authors extracted data from each included study independently according to a standardized protocol.

**Results**

A total of 24 observational studies with 2,103,800 participants (319,568 hip fracture patients) met all the eligibility criteria. Patients with PPIs had a greater risk of hip fracture than those without PPI therapy (RR 1.20, 95% CI 1.14–1.28,  $p < 0.0001$ ). An increased association was also observed in both low and medium doses of PPI taken and hip fracture risk (RR 1.17, 95% CI 1.05–1.29,  $p = 0.002$ ; RR 1.28, 95% CI 1.14–1.44,  $p < 0.0001$ ), but it appeared to be even greater among the patients with higher dose (RR 1.30, 95% CI 1.20–1.40,  $p < 0.0001$ ). Moreover, the overall pooled risk ratios were 1.20 (95% CI 1.15–1.25,  $p < 0.0001$ ) and 1.24 (95% CI 1.10–1.40,  $p < 0.0001$ ) for the patients with short- and long-term PPI therapy, respectively, compared with PPI non-users.

**Conclusion**

Our results suggest that PPI use is significantly associated with an increased risk of hip fracture development, which is not observed in H2RA exposure. Physicians should, therefore, exercise caution when considering a long-term PPI treatment to their patients who already have an elevated risk of hip fracture. In addition, patients should be concerned about the inappropriate use of PPIs; if necessary, then, they should continue to receive it with a clear indication.

## CV risk when exposed to metals and pesticides

Cardiac risk factors and prevention

Original research article

**Association of occupational exposures with cardiovascular disease among US Hispanics/Latinos**

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**Objective** Cardiovascular disease (CVD) is a leading cause of mortality and morbidity in the USA. The role of occupational exposures to chemicals in the development of CVD has rarely been studied even though many agents possess cardiotoxic properties. We therefore evaluated associations of self-reported exposures to organic solvents, metals and pesticides in relation to CVD prevalence among diverse Hispanic/Latino workers.

**Methods** Cross-sectional data from 7404 employed individuals, aged 18–74 years, enrolled in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) were analysed. Participants from four US cities provided questionnaire data and underwent clinical examinations, including ECGs. CVD was defined as the presence of at least one of the following: coronary heart disease, atrial fibrillation, heart failure or cerebrovascular disease. Prevalence ratios reflecting the relationship between each occupational exposure and CVD as well as CVD subtypes were calculated using Poisson regression models.

**Results** Hispanic/Latino workers reported exposures to organic solvents (6.5%), metals (8.5%) and pesticides (4.7%) at their current jobs. Overall, 6.1% of participants had some form of CVD, with coronary heart disease as the most common (4.3%) followed by cerebrovascular disease (1.0%), heart failure (0.8%) and atrial fibrillation (0.7%). For individuals who reported working with pesticides, the prevalence ratios for any CVD were 2.18 (95% CI 1.34 to 3.55), coronary heart disease 2.20 (95% CI 1.31 to 3.71), cerebrovascular disease 1.38 (95% CI 0.62 to 3.03), heart failure 0.91 (95% CI 0.23 to 3.54) and atrial fibrillation 5.92 (95% CI 1.89 to 18.61) after adjustment for sociodemographic, acculturation, lifestyle and occupational characteristics. Metal exposures were associated with an almost fourfold (3.78, 95% CI 1.24 to 11.46) greater prevalence of atrial fibrillation. Null associations were observed for organic solvent exposures.

**Conclusions** Our results suggest that working with metals and pesticides could be risk factors for CVD among Hispanic/Latino workers. Further work is needed to evaluate these relationships prospectively.

### Late night eating habits

#### **Association of night eating habits with metabolic syndrome and its components: A longitudinal study**

BMC Public Health

Yoshida J, et al. | December 12, 2018

In a large Japanese cohort including 40–54 years old 8,153 adults with specific medical checkups done in an Okayama facility from 2009 to 2010 and from 2013 to 2014, researchers evaluated age-adjusted and multivariable-adjusted odds ratios of metabolic syndrome and its components for an average of 3.9 years in relation to night eating habits including dinner immediately before bed, snacks after dinner, or combinations of both. In subjects with both eating habits vs in those with neither habit, the estimated multivariable-adjusted odds ratio for obesity was 2.11 for men and 3.02 for women. Albeit insignificant, a supra-additive interaction influence of both habits on obesity development was seen in women.

Women, not men, showed a link between eating habits at night and metabolic syndrome. Men and women both showed an association of both night eating habits with dyslipidemia. Findings call for intervention and awareness among individuals with night eating habits.



**13 C. AIRWAYS/SWALLOWING/SPEECH****Sleep apnea and BP****Association Between Sleep Apnea and Blood Pressure Control Among Blacks: Jackson Heart Sleep Study**

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. 2018;0

**Background:** Blacks have a high prevalence of hypertension and uncontrolled blood pressure (BP), each of which may be partially explained by untreated sleep apnea. We investigated the association of sleep apnea with uncontrolled BP and resistant hypertension in blacks.

**Methods:** Between 2012 and 2016, Jackson Heart Sleep Study participants (N=913) underwent an in-home Type 3 sleep apnea study, clinic BP measurements, and anthropometry. Moderate or severe obstructive sleep apnea (OSA) was defined as a respiratory event index  $\geq 15$ , and nocturnal hypoxemia was quantified as percent sleep time with  $<90\%$  oxyhemoglobin saturation. Prevalent hypertension was defined as either a systolic BP  $\geq 130$  mm Hg or diastolic BP  $>80$  mm Hg, use of antihypertensive medication, or self-report of a diagnosis of hypertension. Controlled BP was defined as systolic BP  $<130$  mm Hg and diastolic BP  $<80$  mm Hg; uncontrolled BP as systolic BP  $\geq 130$  mm Hg or diastolic BP  $\geq 80$  mm Hg with use of 1 to 2 classes of antihypertensive medication; and resistant BP as systolic BP  $\geq 130$  mm Hg or diastolic BP  $\geq 80$  mm Hg with the use of  $\geq 3$  classes of antihypertensive medication (including a diuretic) or use of  $\geq 4$  classes of antihypertensive medication regardless of BP level. Multinomial logistic regression models were fit to determine the association between OSA severity and uncontrolled BP or resistant hypertension (versus controlled BP) after multivariable adjustment.

**Results:** The analytic sample with hypertension (N=664) had a mean age of 64.0 (SD, 10.6) years, and were predominately female (69.1%), obese (58.6%), and college educated (51.3%). Among the sample, 25.7% had OSA, which was untreated in 94% of participants. Overall, 48% of participants had uncontrolled hypertension and 14% had resistant hypertension. After adjustment for confounders, participants with moderate or severe OSA had a 2.0 times higher odds of resistant hypertension (95% confidence interval [CI], 1.14-3.67). Each standard deviation higher than  $<90\%$  oxyhemoglobin saturation was associated with an adjusted odds ratio for resistant hypertension of 1.25 (95% CI 1.01-1.55). OSA and  $<90\%$  oxyhemoglobin saturation were not associated with uncontrolled BP.

**Conclusions:** Untreated moderate or severe OSA is associated with increased odds of resistant hypertension. These results suggest that untreated OSA may contribute to inadequate BP control in blacks.

**SA and atrial fibrillation****December 2018** Volume 154, Issue 6, Pages 1330–1339**Sleep Apnea Increases the Risk of New Hospitalized Atrial Fibrillation****A Historical Cohort Study**

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DOI: <https://doi.org/10.1016/j.chest.2018.08.1075>

**Objectives**

This study examined the relationship between newly diagnosed OSA and incident hospitalized atrial fibrillation (AF) over the subsequent 10 years in a large arrhythmia-free cohort.

**Methods**

Adults referred between 1994 and 2010 to a large academic hospital with suspected OSA who were arrhythmia-free at the time of the first diagnostic sleep study were included. Clinical data were linked to provincial health administrative data to define outcome. Cox regressions were used to investigate the relationship between severity of OSA as measured by the apnea-hypopnea index (AHI) and degree of nocturnal hypoxemia, and incident hospitalized AF.

**Results**

In total, 8,256 subjects were included in this study. Their median age was 47 years, 62% were men; 28% had an AHI > 30 events per hour, and 6% spent > 30% of sleep time with oxygen saturation < 90%. Over a median follow-up of 10 years (interquartile range, 7-13 years), 173 participants (2.1%) were hospitalized with AF. Controlling for age, sex, alcohol consumption, smoking status, previous heart failure, COPD, and pulmonary embolism, nocturnal hypoxemia (but not AHI) was a significant predictor of incident AF: hazard ratio, 2.47 (95% CI, 1.64-3.71). After further controlling for BMI and hypertension, this association was attenuated but remained significant (hazard ratio, 1.77 [95% CI, 1.15-2.74]).

**Conclusions**

In a large arrhythmia-free clinical cohort with suspected OSA, nocturnal hypoxemia was independently associated with a 77% increased hazard of incident hospitalized AF. These findings further support a relationship between OSA, nocturnal hypoxemia, and new-onset AF, and they may be used to enhance AF prevention in patients with OSA and severe nocturnal hypoxemia.

**Insomnia and CV problems**

Sleep and Breathing pp 1–8

**Insomnia and cardiorespiratory fitness in a middle-aged population: the SCAPIS pilot study**

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**Background**

The relationship between insomnia and cardiorespiratory fitness (CRF), a well-established risk factor for cardiovascular disease, has not been extensively studied. We aimed to assess the independent association between insomnia and CRF in a population-based cohort of subjects aged 50 to 64 years.

**Methods**

Subjects participating in the Swedish CARDioPulmonary bioImaging Study (SCAPIS) pilot cohort ( $n = 603$ , men 47.9%) underwent a submaximal cycle ergometer test for estimation of maximal oxygen consumption ( $VO_2\max$ ). Data on physical activity and sedentary time were collected via waist-worn accelerometers. An insomnia severity index score  $\geq 10$  was used to define insomnia.

**Results**

Insomnia was identified in 31.8% of the population. The  $VO_2\max$  was significantly lower in insomnia subjects compared with the non-insomnia group ( $31.2 \pm 6.3$  vs.  $32.4 \pm 6.5$  ml\* kg<sup>-1</sup> \*min<sup>-1</sup>,  $p = 0.028$ ). There was no difference in objectively assessed physical activity or time spent sedentary between the groups. In a multivariate generalized linear model adjusting for confounders, an independent association between insomnia status and lower  $VO_2\max$  was found in men, but not in women ( $\beta = -1.15$  [95% CI  $-2.23$ – $-0.06$ ] and  $-0.09$  [ $-1.09$ – $0.92$ ],  $p = 0.038$  and  $0.866$ , respectively).

**Conclusions**

We found a modest, but significant, association between insomnia and lower CRF in middle-aged men, but not in women. Our results suggest that insomnia may link to cardiovascular disease via reduced CRF. Insomnia may require a specific focus in the context of health campaigns addressing CRF.

## SA and gout

Arthritis Rheumatol. 2018 Aug 30. doi: 10.1002/art.40662.

**The Risk of Gout Among Patients With Sleep Apnea: A Matched Cohort Study.**

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Author information

Abstract

*OBJECTIVE:*

Obstructive sleep apnea (OSA) is associated with a range of serious comorbidities. This study was undertaken to investigate whether people with OSA are more likely to develop gout, in the short and long term, compared to those without OSA.

*METHODS:*

A matched retrospective cohort study was undertaken using the UK Clinical Practice Research Datalink. Individuals age  $\geq 18$  years who received a diagnosis of OSA between 1990 and 2010 were identified and matched on age, sex, and practice with up to 4 individuals without OSA; follow-up was until the end of 2015. Hazard ratios (HRs) were estimated using Cox regression adjusted for general health, lifestyle, and comorbidity characteristics. The risk of developing gout was assessed at different time points, and the body mass index (BMI) category-specific results were presented.

*RESULTS:*

The study sample included 15,879 patients with OSA and 63,296 without. The median follow-up was 5.8 years. We found that 4.9% of patients with OSA and 2.6% of patients without the disorder developed gout. The incidence rate per 1,000 person-years was 7.83 (95% confidence interval [95% CI] 7.29-8.40) and 4.03 (95% CI 3.84-4.23) among those with and without OSA, respectively. The adjusted HR was 1.42 (95% CI 1.29-1.56). The risk of developing gout among OSA patients compared to those without was highest 1-2 years after the index date (HR 1.64 [95% CI 1.30-2.06]). This finding persisted among those who were overweight and obese. For those with normal BMI, the highest significant HR (2.02 [95% CI 1.13-3.62]) was observed at 2-5 years after the index date.

*CONCLUSION:*

In this study, patients with OSA continued to be at higher risk of developing gout beyond the first year following the diagnosis. Our results further indicate that peak incidences of gout vary according to BMI.

**Light and sleep**

Dement Geriatr Cogn Disord. 2018 Dec 11;46(5-6):371-384. doi: 10.1159/000494921.

**Effects of Light Treatment on Sleep, Cognition, Mood, and Behavior in Alzheimer's Disease: A Systematic Review.**

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**BACKGROUND:**

Bright light treatment is a therapeutic intervention mainly used to treat sleep and circadian disturbances in Alzheimer's disease (AD) patients. Recently, a handful of studies also focused on the effect on cognition and behavior. Conflicting findings are reported in the literature, and no definite conclusions have been drawn about its specific therapeutic effect.

**SUMMARY:**

The aim of this review is to provide a critical evaluation of available evidence in this field, highlighting the specific characteristics of effective bright light treatment. Eligible studies were required to assess at least one of the following outcome measures: sleep, cognition, mood, and/or behavior (e.g., depression, agitation). A total of 32 articles were included in this systematic review and identified as research intervention studies about light treatment in AD. The quality of the papers was evaluated based on the US Preventive Service Task Force guidelines. Key Messages: Overall, the current literature suggests that the effects of light treatment in AD patients are mixed and may be influenced by several factors, but with a general trend toward a positive effect. Bright light seems to be a promising intervention treatment without significant adverse effects; therefore, further well-designed randomized controlled trials are needed taking into account the highlighted recommendations.

## Sleep and CV disease

Eur Heart J. 2018 Dec 5. doi: 10.1093/eurheartj/ehy695.

**Association of estimated sleep duration and naps with mortality and cardiovascular events: a study of 116 632 people from 21 countries.**

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**AIMS:**

To investigate the association of estimated total daily sleep duration and daytime nap duration with deaths and major cardiovascular events.

**METHODS AND RESULTS:**

We estimated the durations of total daily sleep and daytime naps based on the amount of time in bed and self-reported napping time and examined the associations between them and the composite outcome of deaths and major cardiovascular events in 116 632 participants from seven regions. After a median follow-up of 7.8 years, we recorded 4381 deaths and 4365 major cardiovascular events. It showed both shorter ( $\leq 6$  h/day) and longer ( $> 8$  h/day) estimated total sleep durations were associated with an increased risk of the composite outcome when adjusted for age and sex. After adjustment for demographic characteristics, lifestyle behaviours and health status, a J-shaped association was observed. Compared with sleeping 6-8 h/day, those who slept  $\leq 6$  h/day had a non-significant trend for increased risk of the composite outcome [hazard ratio (HR), 1.09; 95% confidence interval, 0.99-1.20]. As estimated sleep duration increased, we also noticed a significant trend for a greater risk of the composite outcome [HR of 1.05 (0.99-1.12), 1.17 (1.09-1.25), and 1.41 (1.30-1.53) for 8-9 h/day, 9-10 h/day, and  $> 10$  h/day,  $P_{\text{trend}} < 0.0001$ , respectively]. The results were similar for each of all-cause mortality and major cardiovascular events. Daytime nap duration was associated with an increased risk of the composite events in those with over 6 h of nocturnal sleep duration, but not in shorter nocturnal sleepers ( $\leq 6$  h).

**CONCLUSION:**

Estimated total sleep duration of 6-8 h per day is associated with the lowest risk of deaths and major cardiovascular events. Daytime napping is associated with increased risks of major cardiovascular events and deaths in those with  $> 6$  h of nighttime sleep but not in those sleeping  $\leq 6$  h/night.

### 14. HEADACHES

#### Job satisfaction

#### **Illness perception and job satisfaction in patients suffering from migraine headaches: Trait anxiety and depressive symptoms as potential mediators**

Headache: The Journal of Head and Face Pain  
Rogante E, et al. | December 14, 2018

Researchers examined the association among illness perception, anxiety, depressive symptoms, and job satisfaction, connected to migraine and its features via analyzing 98 individuals with chronic migraine (CM) treated with OnabotulinumtoxinA from the Regional Referral Headache Centre of Sant'Andrea Hospital in Rome.

The patients were made to complete 4 questionnaires (Brief Illness Perception Quality of Life, Enjoyment and Satisfaction Questionnaire, State-Trait Anxiety Inventory, Beck Depression Inventory-II) and a socio-anamnestic form. They examined 2 mediational models in this cross-sectional study. Trait anxiety displays an indirect mediating effect on the association between illness perception and job satisfaction as per the first model. The second model demonstrate a mediating role of depressive symptoms on the association between illness perception and job satisfaction.

Findings thus suggest the significance of developing interventions to improve the quality of life of individuals with CM and to increase knowledge about headache and psychological consequences.

**20 A. ROTATOR CUFF****MRI effective at finding subscap tears**

Archives of Orthopaedic and Trauma Surgery pp 1–9

**Accuracy of magnetic resonance imaging (MRI) for subscapularis tear: a systematic review and meta-analysis of diagnostic studies**

Eduardo Angeli Malavolta orge Henrique Assunçãoom auro Emilio Conforto Gracitellin Talitha Koo Yen Marcelo Bordalo-Rodrigues Arnaldo Amado Ferreira Neto

**Introduction**

The accuracy of MRI for subscapularis tear is lower than that of overall rotator cuff tears. Until now, no systematic reviews and meta-analysis have been conducted to compile these data. The purpose of this study was to determine, through a systematic review and meta-analysis, the diagnostic accuracy of MRI in the detection of subscapularis tendon tears.

**Materials and methods**

A systematic review of PubMed, EMBASE, and MEDLINE databases up to April 2017 was performed. All studies assessing the sensitivity and specificity of the MRI (index test) compared to arthroscopic surgical findings (reference test) for subscapularis tendon tear were included. A meta-analysis was performed to calculate pooled sensitivity, specificity, sROC curve, and diagnostic odds ratio values.

**Results**

A total of 497 citations were identified. After applying the eligibility criteria, 14 articles were included, including 1858 shoulders with 613 subscapularis tears. For overall subscapularis tears, sensitivity was 0.68 (95% CI 0.64–0.72) and specificity was 0.90 (95% CI 0.89–0.92). Sensitivity was 0.93 (95% CI 0.83–0.98) for full-thickness tears and 0.74 (95% CI 0.66–0.82) for partial tears. Specificity was 0.97 (95% CI 0.94–0.98) for full-thickness tears and 0.88 (95% CI 0.85–0.91) for partial tears. Analyzing only studies with field of strength  $\geq 1.5$  T, sensitivity was 0.80 (95% CI 0.76–0.84) and specificity 0.84 (95% CI 0.81–0.87).

**Conclusion**

MRI is an accurate method for diagnosing subscapularis tendon tears; however, its accuracy is lower than that of overall rotator cuff tears, due to its lower sensitivity.



### 35. KNEE/TOTAL

#### Renal problems

#### **Preoperative eGFR is a marker for postoperative complications following revision total knee arthroplasty**

Journal of Arthroplasty — Cohen JS, et al. | December 11, 2018

Experts evaluated the impact of less severe, but clinically significant, renal impairment following revision total knee arthroplasty.

They conducted a retrospective cohort study using the American College of Surgeons National Quality Improvement Program Database. Greater risk for many postoperative complications is seen in the patients with decreased eGFRs, but this increased risk is generally associated with the greater number of comorbidities in this patient population.

When controlling for these comorbidities, an independent risk factor for extended length of stay as well as postoperative renal injury and renal failure is poor renal function, and patients may benefit from perioperative measures to limit this excess renal risk.

**48 A. STM****Massage helps knee OA**

Journal of General Internal Medicine pp 1–8|

**Efficacy and Safety of Massage for Osteoarthritis of the Knee: a Randomized Clinical Trial**

Adam Perlman Susan Gould Fogerite David L. Katz

**Background** Current treatment options for knee osteoarthritis have limited effectiveness and potentially adverse side effects. Massage may offer a safe and effective complement to the management of knee osteoarthritis.

**Objective** Examine effects of whole-body massage on knee osteoarthritis, compared to active control (light-touch) and usual care.

**Design** Multisite RCT assessing the efficacy of massage compared to light-touch and usual care in adults with knee osteoarthritis, with assessments at baseline and weeks 8, 16, 24, 36, and 52. Subjects in massage or light-touch groups received eight weekly treatments, then were randomized to biweekly intervention or usual care to week 52. The original usual care group continued to week 24. Analysis was performed on an intention-to-treat basis.

**Participants** Five hundred fifty-one screened for eligibility, 222 adults with knee osteoarthritis enrolled, 200 completed 8-week assessments, and 175 completed 52-week assessments.

**Intervention** Sixty minutes of protocolized full-body massage or light-touch.

**Main Measures** Primary: Western Ontario and McMaster Universities Arthritis Index. Secondary: visual analog pain scale, PROMIS Pain Interference, knee range of motion, and timed 50-ft walk.

**Key Results**

At 8 weeks, massage significantly improved WOMAC Global scores compared to light-touch ( $-8.16$ , 95% CI =  $-13.50$  to  $-2.81$ ) and usual care ( $-9.55$ , 95% CI =  $-14.66$  to  $-4.45$ ). Additionally, massage improved pain, stiffness, and physical function WOMAC subscale scores compared to light-touch ( $p < 0.001$ ;  $p = 0.04$ ;  $p = 0.02$ , respectively) and usual care ( $p < 0.001$ ;  $p = 0.002$ ;  $p = 0.002$ ; respectively). At 52 weeks, the omnibus test of any group difference in the change in WOMAC Global from baseline to 52 weeks was not significant ( $p = 0.707$ ,  $df = 3$ ), indicating no significant difference in change across groups. Adverse events were minimal.

**Conclusions** Efficacy of symptom relief and safety of weekly massage make it an attractive short-term treatment option for knee osteoarthritis. Longer-term biweekly dose maintained improvement, but did not provide additional benefit beyond usual care post 8-week treatment.

**52. EXERCISE****Endurance benefits****Differential effects of endurance, interval, and resistance training on telomerase activity and telomere length in a randomized, controlled study.**

Werner CM, et al. Eur Heart J. 2018.

**Abstract**

**Aims:** It is unknown whether different training modalities exert differential cellular effects. Telomeres and telomere-associated proteins play a major role in cellular aging with implications for global health. This prospective training study examines the effects of endurance training, interval training (IT), and resistance training (RT) on telomerase activity and telomere length (TL).

**Methods and results:** One hundred and twenty-four healthy previously inactive individuals completed the 6 months study. Participants were randomized to three different interventions or the control condition (no change in lifestyle): aerobic endurance training (AET, continuous running), high-intensive IT (4 × 4 method), or RT (circle training on 8 devices), each intervention consisting of three 45 min training sessions per week. Maximum oxygen uptake (VO<sub>2</sub>max) was increased by all three training modalities. Telomerase activity in blood mononuclear cells was up-regulated by two- to three-fold in both endurance exercise groups (AET, IT), but not with RT. In parallel, lymphocyte, granulocyte, and leucocyte TL increased in the endurance-trained groups but not in the RT group. Magnet-activated cell sorting with telomerase repeat-amplification protocol (MACS-TRAP) assays revealed that a single bout of endurance training-but not RT- acutely increased telomerase activity in CD14<sup>+</sup> and in CD34<sup>+</sup> leucocytes.

**Conclusion :** This randomized controlled trial shows that endurance training, IT, and RT protocols induce specific cellular pathways in circulating leucocytes. Endurance training and IT, but not RT, increased telomerase activity and TL which are important for cellular senescence, regenerative capacity, and thus, healthy aging.

### 53. CORE

#### Sarcopenia

##### **The association of back muscle strength and sarcopenia-related parameters in the patients with spinal disorders**

European Spine Journal

Toyoda H, et al. | December 13, 2018

Researchers performed this cross-sectional observational study including 230 consecutive patients with spinal disorders who visited their outpatient clinic (age range 65–92 years) to evaluate the association between back muscle strength, trunk muscle mass, and sarcopenia-related parameters in these patients.

Significant correlation of back muscle strength was noted with trunk muscle mass, handgrip strength, and gait speed. Sarcopenia, dynapenia, and normal stages were noted in 16.4%, 26.7%, and 56.9% for males, and 23.7%, 50.9%, and 25.4% for females, respectively. Females displayed a significantly higher prevalence of dynapenia than males. The normal group had back muscle strength significantly greater than that observed in the sarcopenic and dynapenic groups.

**59. PAIN****Pain in African Americans****Racial-Ethnic Differences in Osteoarthritis Pain and Disability: A Meta-Analysis**

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DOI: <https://doi.org/10.1016/j.jpain.2018.11.012>

**Highlights**

- WOMAC was the most commonly used clinical pain scale.
- Clinical pain severity was higher amongst African Americans than Caucasians.
- African-Americans also reported higher disability and lower physical performance

**Abstract**

Osteoarthritis (OA), a leading cause of disability and pain, affects 32.5 million Americans, producing tremendous economic burden. While some findings suggest that racial/ethnic minorities experience increased OA pain severity, other studies have shown conflicting results. This meta-analysis examined differences in clinical pain severity between African Americans and Non-Hispanic Whites with osteoarthritis. Articles were initially identified October 1-5, 2016, and updated May 30, 2018 using PubMed®, Web of Science™, PsycINFO, and the Cochrane Library. Eligibility included English-language peer-reviewed articles comparing clinical pain severity in adult Black/African American and Non-Hispanic White/Caucasian patients with osteoarthritis. Non-duplicate article abstracts (N=1,194) were screened by four reviewers, 224 articles underwent full text review, and 61 articles reported effect sizes of pain severity stratified by race. Forest plots of standard mean difference showed higher pain severity in African-Americans for studies using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (0.57; 95%CI: 0.54, 0.61) and non-WOMAC studies (0.35; 95%CI: 0.23, 0.47). African-Americans also showed higher self-reported disability (0.38; 95%CI: 0.22, 0.54) and poorer performance testing (-0.58; 95%CI: -0.72, -0.44). Clinical pain severity and disability in OA is higher amongst African Americans and future studies should explore the reasons for these differences to improve pain management.

**Perspective**

This meta-analysis shows that differences exist in clinical pain severity, functional limitations and poor performance between African Americans and Non-Hispanic Whites with osteoarthritis. This research may lead to better understanding of racial/ethnic differences in OA-related pain.

**Bullying and chronic pain****Associations of adverse childhood experiences and bullying on physical pain in the general population of Germany**

**Authors** Brown RC, Plener PL, Braehler E, Fegert JM, Huber-Lang M

**DOI** <https://doi.org/10.2147/JPR.S169135>

**Background:** Chronic pain is a frequent burden in the general population. Child maltreatment and bullying are risk factors for the development of chronic pain. Aim of this cross-sectional study was to investigate the association of child maltreatment and bullying and pain experiences in a representative sample of the general population.

**Materials and methods:** A total of N=2,491 people from the general population of Germany participated in the study ( $M_{age}=48.3$  years [SD=18.2], 53.2 % female). Child maltreatment was assessed with the Childhood Trauma Questionnaire (CTQ), pain was rated with the Polytrauma Outcome (POLO)-physical state domain, depression scores were assessed with the Patient Health Questionnaire, and anxiety scores via the General Anxiety Disorder Questionnaire. Regression analyses were calculated to investigate the effect of bullying and child maltreatment, as well as depression, anxiety, and gender on pain experiences.

**Results:** A significant correlation between increasing pain levels and number of adverse childhood experiences was found. With regard to specific types of maltreatment, largest effect sizes were found for emotional abuse. Bullying was significantly, but overall rather moderately, related to pain suffering. In women, all forms of maltreatment were associated with pain, while in men only sexual and physical abuse revealed significant effects. Although depression and anxiety scores were significantly associated with the experience of current pain, they did not change the effect of child maltreatment on pain significantly.

**Conclusion:** In this sample of the general population, adverse childhood experiences were significantly associated with pain and showed cumulative effects, over and above depressive and anxiety symptoms.

## 61. FIBROMYALGIA

### Intercranial pressure

#### **The link between idiopathic intracranial hypertension, fibromyalgia, and chronic fatigue syndrome: exploration of a shared pathophysiology**

**Authors** Hulens M, Rasschaert R, Vansant G, Stalmans I, Bruyninckx F, Dankaerts W

**DOI** <https://doi.org/10.2147/JPR.S186878>

**Purpose:** Idiopathic intracranial hypertension (IICH) is a condition characterized by raised intracranial pressure (ICP), and its diagnosis is established when the opening pressure measured during a lumbar puncture is elevated  $>20$  cm H<sub>2</sub>O in nonobese patients or  $>25$  cm H<sub>2</sub>O in obese patients. Papilledema is caused by forced filling of the optic nerve sheath with cerebrospinal fluid (CSF). Other common but underappreciated symptoms of IICH are neck pain, back pain, and radicular pain in the arms and legs resulting from associated increased spinal pressure and forced filling of the spinal nerves with CSF. Widespread pain and also several other characteristics of IICH share notable similarities with characteristics of fibromyalgia (FM) and chronic fatigue syndrome (CFS), two overlapping chronic pain conditions. The aim of this review was to compare literature data regarding the characteristics of IICH, FM, and CFS and to link the shared data to an apparent underlying physiopathology, that is, increased ICP.

**Methods:** Data in the literature regarding these three conditions were compared and linked to the hypothesis of the shared underlying physiopathology of increased cerebrospinal pressure.

**Results:** The shared characteristics of IICH, FM, and CFS that can be caused by increased ICP include headaches, fatigue, cognitive impairment, loss of gray matter, involvement of cranial nerves, and overload of the lymphatic olfactory pathway. Increased pressure in the spinal canal and in peripheral nerve root sheaths causes widespread pain, weakness in the arms and legs, walking difficulties (ataxia), and bladder, bowel, and sphincter symptoms. Additionally, IICH, FM, and CFS are frequently associated with sympathetic overactivity symptoms and obesity. These conditions share a strong female predominance and are frequently associated with Ehlers-Danlos syndrome.

**Conclusion:** IICH, FM, and CFS share a large variety of symptoms that might all be explained by the same pathophysiology of increased cerebrospinal pressure.

### 62 A. NUTRITION/VITAMINS

#### Fx risk increases with use of NSAID'S

#### **Nonsteroidal anti-inflammatory drug prescriptions are associated with increased stress fracture diagnosis in the US Army population**

Journal of Bone and Mineral Research  
Hughes JM, et al. | December 12, 2018

Among US Army soldiers, researchers ascertained if prescribed nonsteroidal anti-inflammatory drugs (NSAIDs) were associated with stress fracture diagnoses.

They also examined whether acetaminophen, an analgesic alternative to NSAIDs, was linked to the risk of stress fractures. Using data from the Total Army Injury and Health Outcomes Database from 2002 to 2011 (n = 1,260,168), a nested case-control study was conducted. During basic combat training (BCT), the risk was more than 5-fold greater in soldiers prescribed NSAIDs and more than 4-fold greater in soldiers prescribed acetaminophen. Findings revealed that NSAID prescription was related to a 2.9-fold increase and acetaminophen prescription with a 2.1-fold increase in stress fracture risk within the total Army population.

Particularly during periods of heightened physical activity, an association was found between NSAID and acetaminophen prescriptions and stress fracture risk.