

## 2. LBP

### Opioid use and LBP

The Journal of Pain

#### **Prescription Medication Use among Community-Based US Adults with Chronic Low Back Pain: a Cross-Sectional Population Based Study.**

- Anna Shmigel, MD MSc<sup>1,2</sup>, Linh Ngo, DO<sup>2</sup>, Kristine Ensrud, MD MPH<sup>3</sup>, Robert Foley, MD<sup>4</sup>

<https://doi.org/10.1016/j.jpain.2018.04.004>

#### Highlights

- Opioids were the most common prescription pain medications among US adults with cLBP.
- Opioids were typically used long-term, and combined with other CNS-active agents.
- Low level of education was strongly associated with opioid use in cLBP population.

#### **Abstract.**

Many classes of medications have been evaluated in chronic low back pain (cLBP), however their utilization in the community remains unclear. We examine patterns of prescription medication use among Americans with cLBP in a nationally representative, community-based sample. The Back Pain Survey was administered to a representative sample of US adults aged 20-69 (N = 5103) during the 2009-2010 cycle of the National Health and Nutrition Examination Survey (NHANES). cLBP was defined as self-reported pain in the area between the lower posterior margin of the ribcage and the horizontal gluteal fold on most days for at least 3 months (N = 700). Home-based interviews with pill bottle verification were used to capture commonly prescribed medications for chronic pain. Among the sample of US adults with cLBP aged 20-69, 36.9% took at least one prescription pain medication in the past 30 days. 18.8% used opioids, 9.7% NSAIDs, 8.5% muscle relaxants, 6.9% gabapentin or pregabalin. Non-pain antidepressants and hypnotics were used by 17.8% and 4.7%, respectively. Opioids were used long-term in 76.9% of cases (median 2 years) and were frequently co-administered with antidepressants, benzodiazepines, or hypnotics. 94% of prescription opioids in the cLBP population were used by subjects with less than a college education. Opioids were the most widely used prescription analgesic class in community-based US adults with cLBP and were often co-administered with other CNS-active medications. Opioid use was highly prevalent among less educated Americans with cLBP.

#### *Perspective*

. As prescription opioid use is an issue of national concern, we examined pain-related prescription medication use in community-dwelling among US adults with cLBP. Opioids were the most common prescription pain medication, typically used long-term, in combination with other CNS-active agents, and disproportionately among subjects with less than a college education.

**A good look at the problem**

Lancet. 2018 Mar 20. pii: S0140-6736(18)30480-X. doi: 10.1016/S0140-6736(18)30480-X.

**What low back pain is and why we need to pay attention.**

Hartvigsen J<sup>1</sup>, Hancock MJ<sup>2</sup>, Kongsted A<sup>1</sup>, Louw Q<sup>3</sup>, Ferreira ML<sup>4</sup>, Genevay S<sup>5</sup>, Hoy D<sup>6</sup>, Karppinen J<sup>7</sup>, Pransky G<sup>8</sup>, Sieper J<sup>9</sup>, Smeets RJ<sup>10</sup>, Underwood M<sup>11</sup>;

Low back pain is a very common symptom. It occurs in high-income, middle-income, and low-income countries and all age groups from children to the elderly population. Globally, years lived with disability caused by low back pain increased by 54% between 1990 and 2015, mainly because of population increase and ageing, with the biggest increase seen in low-income and middle-income countries. Low back pain is now the leading cause of disability worldwide. For nearly all people with low back pain, it is not possible to identify a specific nociceptive cause. Only a small proportion of people have a well understood pathological cause-eg, a vertebral fracture, malignancy, or infection. People with physically demanding jobs, physical and mental comorbidities, smokers, and obese individuals are at greatest risk of reporting low back pain. Disabling low back pain is over-represented among people with low socioeconomic status. Most people with new episodes of low back pain recover quickly; however, recurrence is common and in a small proportion of people, low back pain becomes persistent and disabling.

Initial high pain intensity, psychological distress, and accompanying pain at multiple body sites increases the risk of persistent disabling low back pain. Increasing evidence shows that central pain-modulating mechanisms and pain cognitions have important roles in the development of persistent disabling low back pain.

Cost, health-care use, and disability from low back pain vary substantially between countries and are influenced by local culture and social systems, as well as by beliefs about cause and effect. Disability and costs attributed to low back pain are projected to increase in coming decades, in particular in low-income and middle-income countries, where health and other systems are often fragile and not equipped to cope with this growing burden. Intensified research efforts and global initiatives are clearly needed to address the burden of low back pain as a public health problem.

PMID: 29573870 DOI: 10.1016/S0140-6736(18)30480-X

### A call for action

Lancet. 2018 Mar 20. pii: S0140-6736(18)30488-4. doi: 10.1016/S0140-6736(18)30488-4

#### **Low back pain: a call for action.**

Buchbinder R<sup>1</sup>, van Tulder M<sup>2</sup>, Öberg B<sup>3</sup>, Costa LM<sup>4</sup>, Woolf A<sup>5</sup>, Schoene M<sup>6</sup>, Croft P<sup>7</sup>;

Low back pain is the leading worldwide cause of years lost to disability and its burden is growing alongside the increasing and ageing population.<sup>1</sup> Because these population shifts are more rapid in low-income and middle-income countries, where adequate resources to address the problem might not exist, the effects will probably be more extreme in these regions. Most low back pain is unrelated to specific identifiable spinal abnormalities, and our Viewpoint, the third paper in this Lancet Series,<sup>2,3</sup> is a call for action on this global problem of low back pain.

PMID: 29573871 DOI: 10.1016/S0140-6736(18)30488-4

### Management strategies

#### Prevention and treatment of low back pain: evidence, challenges, and promising directions

Prof Nadine E Foster, DPhil Prof Johannes R Anema, PhD Dan Cherkin, PhD Prof Roger Chou, PhD Prof Steven P Cohen, MD Prof Douglas P Gross, PhD Paulo H Ferreira, PhD Prof Julie M Fritz, PhD Prof Bart W Koes, PhD Prof Wilco Peul, PhD Prof Judith A Turner, PhD Prof Chris G Maher, PhD

DOI: [https://doi.org/10.1016/S0140-6736\(18\)30489-6](https://doi.org/10.1016/S0140-6736(18)30489-6)

|

#### Summary

Many clinical practice guidelines recommend similar approaches for the assessment and management of low back pain. Recommendations include use of a biopsychosocial framework to guide management with initial non-pharmacological treatment, including education that supports self-management and resumption of normal activities and exercise, and psychological programmes for those with persistent symptoms.

Guidelines recommend prudent use of medication, imaging, and surgery. The recommendations are based on trials almost exclusively from high-income countries, focused mainly on treatments rather than on prevention, with limited data for cost-effectiveness. However, globally, gaps between evidence and practice exist, with limited use of recommended first-line treatments and inappropriately high use of imaging, rest, opioids, spinal injections, and surgery. Doing more of the same will not reduce back-related disability or its long-term consequences. The advances with the greatest potential are arguably those that align practice with the evidence, reduce the focus on spinal abnormalities, and ensure promotion of activity and function, including work participation. We have identified effective, promising, or emerging solutions that could offer new directions, but that need greater attention and further research to determine if they are appropriate for large-scale implementation.

These potential solutions include focused strategies to implement best practice, the redesign of clinical pathways, integrated health and occupational interventions to reduce work disability, changes in compensation and disability claims policies, and public health and prevention strategies.

## 6. PELVIC GIRDLE

### IBS and SI pain

Arthritis Care Res (Hoboken). 2017 Jul 21. doi: 10.1002/acr.23323.

#### **Prevalence of Sacroiliitis in Inflammatory Bowel Disease Using a Standardized Computed Tomography Scoring System.**

Chan J<sup>1</sup>, Sari I<sup>2</sup>, Salonen D<sup>3</sup>, Silverberg MS<sup>4</sup>, Haroon N<sup>5</sup>, Inman RD<sup>5</sup>.

#### *OBJECTIVE:*

There is an increasing emphasis on the early identification and treatment of ankylosing spondylitis (AS) of which the hallmark is sacroiliitis. Patients with inflammatory bowel disease (IBD) are at increased risk of AS and often receive computed tomography (CT) scans of their abdomen, affording clinicians the opportunity to determine the presence of sacroiliitis. Previous studies using CT have relied only on the radiologist's gestalt or a nonvalidated adaptation of the modified New York criteria. Our aim is to assess the prevalence of sacroiliitis in IBD using a validated screening tool and to determine how frequently these patients are referred for rheumatologic evaluation.

#### *METHODS:*

Patients with IBD were recruited from an IBD clinic. Control patients were recruited from a urology clinic and were confirmed to be without back pain, spondylitis, psoriasis, colitis, or uveitis by chart review. CT scans were read by 2 blinded readers and sacroiliitis was defined by the presence of ankylosis or a total erosion score of  $\geq 3$ .

#### *RESULTS:*

CT scans were available in 233 Crohn's disease (CD) patients, 83 ulcerative colitis (UC) patients, and 108 control patients, and sacroiliitis was seen in 15%, 16.9%, and 5.6% of patients, respectively. The prevalence was higher in patients with IBD than in controls ( $P = 0.007$ ), with no significant difference between CD and UC patients. Of the 49 IBD patients found to have sacroiliitis by CT scan, only 5 had been referred to a rheumatologist.

#### *CONCLUSION:*

There is a 3-fold higher prevalence of sacroiliitis in IBD compared with controls. Despite a growing awareness of this increased prevalence, many patients are not referred to a rheumatologist.

## 7. PELVIC ORGANS/WOMAN'S HEALTH

### C section

Am J Obstet Gynecol. 2018 Apr 12. pii: S0002-9378(18)30293-X. doi: 10.1016/j.ajog.2018.04.012

#### **Cesarean Delivery in the United States 2005 - 2014: A Population-Based Analysis Using the Robson Ten Group Classification System.**

Hehir MP<sup>1</sup>, Ananth CV<sup>2</sup>, Siddiq Z<sup>3</sup>, Flood K<sup>4</sup>, Friedman AM<sup>3</sup>, D'Alton ME<sup>3</sup>.

#### *BACKGROUND:*

Cesarean delivery has increased steadily in the United States over recent decades with significant downstream health consequences. The World Health Organization has endorsed the Robson Ten Group Classification System (TGCS) as a global standard to facilitate analysis and comparison of cesarean delivery rates.

#### *OBJECTIVE:*

Our objective was to apply the TGCS to a nationwide cohort in the United States over a 10-year period.

#### *STUDY DESIGN:*

This population-based analysis applied the TGCS to all births in the United States from 2005-2014, recorded in the 2003-revised birth certificate format. Over the study 10-year period 27,044,217 deliveries met inclusion criteria. Five parameters (parity including previous cesarean, gestational age, labor onset, fetal presentation and plurality), identifiable on presentation for delivery, were used to classify all women included into one of ten groups.

#### *RESULTS:*

The overall cesarean rate was 31.6%. Group 3 births (singleton, term, cephalic multiparas in spontaneous labor) were most common, while Group 5 births (those with a previous cesarean) accounted for the most cesarean deliveries increasing from 27% of all cesareans in 2005-06 to over 34% in 2013-14. Breech pregnancies (Groups 6 and 7) had cesarean rates above 90%. Primiparous and multiparous women who had a prelabor cesarean [Groups 2(b) and 4(b)] accounted for over one quarter of all cesarean deliveries.

#### *CONCLUSION:*

Women with a previous cesarean delivery represent an increasing proportion of cesarean deliveries. Use of the Robson criteria allows standardised comparisons of data and identifies clinical scenarios driving changes in cesarean rates. Hospitals and health organisations can use the TGCS to evaluate quality and processes associated with cesarean delivery.

**Lubricant use**

BJOG. 2018 Mar 15. doi: 10.1111/1471-0528.15218.

**Lubricant use during intercourse and time to pregnancy: a prospective cohort study.**

McInerney KA<sup>1</sup>, Hahn KA<sup>1</sup>, Hatch EE<sup>1</sup>, Mikkelsen EM<sup>2</sup>, Steiner AZ<sup>3</sup>, Rothman KJ<sup>1,4</sup>, Sørensen HT<sup>1,2</sup>, Snerum TM<sup>5</sup>, Wise LA<sup>1</sup>.

**OBJECTIVE:**

To assess the extent to which lubricant use during intercourse is associated with time to pregnancy (TTP).

**DESIGN:**

Prospective cohort study.

**SETTING:**

Denmark and North America.

**POPULATION:**

A total of 6467 women aged 18-49 years who were not using contraception or fertility treatment.

**METHODS:**

We pooled data from two continuing prospective cohort studies of pregnancy planners in Denmark (2011-2017) and North America (2013-2017). Female participants completed bimonthly questionnaires for 12 months or until they reported pregnancy. After restricting the study to women without a history of infertility who had been trying to conceive for six or fewer cycles at enrollment, 6467 women were retained for analysis. Self-reported lubricant use was categorised as water-based/not pH balanced, water-based/pH balanced 'fertility friendly', silicone-based, oil-based, or a combination of these. We used proportional probability models to calculate fecundability ratios (FRs) and 95% confidence intervals (95% CIs) for the association between lubricant use and fecundability, after adjusting for cohort and sociodemographic and lifestyle factors.

**MAIN OUTCOME MEASURE:**

Fecundability.

**RESULTS:**

At baseline, 17.5% of participants reported the use of lubricants, most commonly water-based/not pH balanced (11.4%). Compared with non-use of lubricants, FRs were 1.02 (95% CI 0.93-1.11) for water-based/not pH-balanced lubricant use, 1.01 (95% CI 0.86-1.18) for water-based/pH balanced 'fertility friendly' lubricant use, 1.23 (95% CI 0.94-1.61) for oil-based lubricant use, and 1.27 (95% CI 0.93-1.73) for silicone-based lubricant use. Associations between oil-based lubricant use and fecundability were inconsistent across subgroups of study cohort, age, parity, and intercourse frequency.

**CONCLUSIONS:**

Lubricant use was not associated with reduced fecundability in the preconception cohorts of pregnancy planners studied.

**Vaginal birth after C section**

BMC Pregnancy Childbirth. 2018 Apr 11;18(1):92. doi: 10.1186/s12884-018-1720-6.

**Vaginal birth after caesarean versus elective repeat caesarean delivery after one previous caesarean section: a cost-effectiveness analysis in four European countries.**

Fobelets M<sup>1,2</sup>, Beeckman K<sup>3,4</sup>, Faron G<sup>5</sup>, Daly D<sup>6</sup>, Begley C<sup>6,7</sup>, Putman K<sup>8,3</sup>.

*BACKGROUND:*

The OptiBIRTH study incorporates a multicentre cluster randomised trial in 15 hospital sites across three European countries. The trial was designed to test a complex intervention aimed at improving vaginal birth after caesarean section (VBAC) rates through increasing women's involvement in their care. Prior to developing a robust standardised model to conduct the health economic analysis, an analysis of a hypothetical cohort was performed to estimate the costs and health effects of VBAC compared to elective repeat caesarean delivery (ERCD) for low-risk women in four European countries.

*METHODS:*

A decision-analytic model was developed to estimate the costs and the health effects, measured using Quality Adjusted Life Years (QALYs), of VBAC compared with ERCD. A cost-effectiveness analysis for the period from confirmation of pregnancy to 6 weeks postpartum was performed for short-term consequences and during lifetime for long-term consequences, based on a hypothetical cohort of 100,000 pregnant women in each of four different countries; Belgium, Germany, Ireland and Italy. A societal perspective was adopted. Where possible, transition probabilities, costs and health effects were adapted from national data obtained from the respective countries. Country-specific thresholds were used to determine the cost-effectiveness of VBAC compared to ERCD. Deterministic and probabilistic sensitivity analyses were conducted to examine the uncertainty of model assumptions.

*RESULTS:*

Within a 6-week time horizon, VBAC resulted in a reduction in costs, ranging from €3,334,052 (Germany) to €66,162,379 (Ireland), and gains in QALYs ranging from 6399 (Italy) to 7561 (Germany) per 100,000 women birthing in each country. Compared to ERCD, VBAC is the dominant strategy in all four countries. Applying a lifetime horizon, VBAC is dominant compared to ERCD in all countries except for Germany (probabilistic analysis, ICER: €8609/QALY). In conclusion, compared to ERCD, VBAC remains cost-effective when using a lifetime time.

*CONCLUSIONS:*

In all four countries, VBAC was cost-effective compared to ERCD for low-risk women. This is important for health service managers, economists and policy makers concerned with maximising health benefits within limited and constrained resources.



**Dilatation**

BJOG. 2018 Mar 2. doi: 10.1111/1471-0528.15205. [

**Cervical dilatation over time is a poor predictor of severe adverse birth outcomes: a diagnostic accuracy study.**

Souza JP<sup>1</sup>, Oladapo OT<sup>1</sup>, Fawole B<sup>2</sup>, Mugerwa K<sup>3</sup>, Reis R<sup>4</sup>, Barbosa-Junior F<sup>4</sup>, Oliveira-Ciabati L<sup>4</sup>, Alves D<sup>4</sup>, Gülmezoglu AM<sup>1</sup>.

**OBJECTIVE:**

To assess the accuracy of the World Health Organization (WHO) partograph alert line and other candidate predictors in the identification of women at risk of developing severe adverse birth outcomes.

**DESIGN:**

A facility-based, multicentre, prospective cohort study.

**SETTING:**

Thirteen maternity hospitals located in Nigeria and Uganda.

**POPULATION:**

A total of 9995 women with spontaneous onset of labour presenting at cervical dilatation of  $\leq 6$  cm or undergoing induction of labour.

**METHODS:**

Research assistants collected data on sociodemographic, anthropometric, obstetric, and medical characteristics of study participants at hospital admission, multiple assessments during labour, and interventions during labour and childbirth. The alert line and action line, intrapartum monitoring parameters, and customised labour curves were assessed using sensitivity, specificity, positive and negative likelihood ratios, diagnostic odds ratio, and the J statistic.

**OUTCOMES:**

Severe adverse birth outcomes.

**RESULTS:**

The rate of severe adverse birth outcomes was 2.2% (223 women with severe adverse birth outcomes), the rate of augmentation of labour was 35.1% (3506 women), and the caesarean section rate was 13.2% (1323 women). Forty-nine percent of women in labour crossed the alert line (4163/8489). All reference labour curves had a diagnostic odds ratio ranging from 1.29 to 1.60. The J statistic was less than 10% for all reference curves.

**CONCLUSIONS:**

Our findings suggest that labour is an extremely variable phenomenon, and the assessment of cervical dilatation over time is a poor predictor of severe adverse birth outcomes. The validity of a partograph alert line based on the 'one-centimetre per hour' rule should be re-evaluated.

**Vaginal microbial**

Menopause. 2018 May;25(5):500-507. doi: 10.1097/GME.0000000000001037.

**Associations between improvement in genitourinary symptoms of menopause and changes in the vaginal ecosystem.**

Mitchell CM<sup>1,2</sup>, Srinivasan S<sup>3</sup>, Plantinga A<sup>4</sup>, Wu MC<sup>3</sup>, Reed SD<sup>3,5</sup>, Guthrie KA<sup>3</sup>, LaCroix AZ<sup>6</sup>, Fiedler T<sup>3</sup>, Munch M<sup>3</sup>, Liu C<sup>3</sup>, Hoffman NG<sup>7</sup>, Blair IA<sup>8</sup>, Newton K<sup>9</sup>, Freeman EW<sup>10</sup>, Joffe H<sup>2,11</sup>, Cohen L<sup>2,12</sup>, Fredricks DN<sup>3</sup>.

**OBJECTIVE:**

The aim of the study was to identify associations between improvement in genitourinary symptoms of menopause (GSM) and vaginal microbiota, vaginal glycogen, and serum estrogen.

**METHODS:**

Thirty postmenopausal women enrolled in a hot flash treatment trial (oral estradiol vs venlafaxine vs placebo) who reported GSM and provided vaginal swabs at 0, 4, and 8 weeks were studied. Bacterial communities were characterized using deep sequencing targeting the 16S rRNA gene V3-V4 region. Participants selected a most bothersome genitourinary symptom (dryness, discharge, pain, itch/burn, or inability to have sex) and rated severity on a 10-point scale at baseline and 8 weeks. Vaginal glycogen and serum estradiol and estrone were measured at enrollment and 8 weeks. Comparisons according to improvement in most bothersome symptom (MBS) were made using  $\chi$ , Wilcoxon signed-rank test, or Hotelling's t test.

**RESULTS:**

Of 30 participants, 21 (70%) had improvement in MBS over the 8-week study and 9 (30%) had no improvement or worsening of MBS. A higher proportion of women receiving estradiol or venlafaxine reported improvement in MBS (88%, 78%) compared with placebo (54%;  $P=0.28$ ). MBS improvement was associated with Lactobacillus-dominant vaginal microbiota at enrollment (57% vs 22%,  $P=0.08$ ). Vaginal glycogen, serum estradiol, and estrone significantly increased in women whose MBS improved.

**CONCLUSIONS:**

A larger proportion of women whose MBS improved had a Lactobacillus dominant microbiota at enrollment than those who had no improvement during the trial, though this difference was not statistically significant. Larger trials are needed to determine whether vaginal microbiota modify or mediate treatment responses in women with GSM.

**Antibiotic use and childhood asthma**

Eur Respir J. 2018 Apr 20. pii: 1702070. doi: 10.1183/13993003.02070-2017. [

**Prenatal antibiotic exposure and childhood asthma: a population-based study.**

Loewen K<sup>1,2</sup>, Monchka B<sup>3,4</sup>, Mahmud SM<sup>3,4,5</sup>, Jong G<sup>1,6,7</sup>, Azad MB<sup>1,5,6</sup>.

Antibiotic use during infancy alters gut microbiota and immune development and is associated with an increased risk of childhood asthma. The impact of prenatal antibiotic exposure is unclear.

We sought to characterise the association between prenatal antibiotic exposure and childhood asthma. We performed a population-based cohort study using prescription records, hospitalization records, and physician billing claims from 213,661 mother-child dyads born in Manitoba, Canada from 1996-2012. Associations were determined using Cox regression, adjusting for maternal asthma, postnatal antibiotics, and other potential confounders. Sensitivity analyses evaluated maternal antibiotic use before and after pregnancy. 36.8% of children were prenatally exposed to antibiotics, and 10.1% developed asthma. Prenatal antibiotic exposure was associated with an increased risk of asthma (adjusted HR 1.23, 95%CI 1.20-1.27). There was an apparent dose-response (aHRs: 1.15, 1.11-1.18 for 1 course; 1.26, 1.21-1.32 for 2 courses; 1.51, 1.44-1.59 for  $\geq 3$  courses). Maternal antibiotic use during 9 months before pregnancy (1.27, 1.24-1.31) and 9 months postpartum (1.32, 1.28-1.36) were similarly associated with asthma.

Prenatal antibiotic exposure was associated with a dose-dependent increase in asthma risk. However, similar associations were observed for maternal antibiotic use before and after pregnancy, suggesting the association is either not directly causal, or not specific to pregnancy.

**Asthma and maternal smoking**

Pediatr Allergy Immunol. 2018 Mar 7. doi: 10.1111/pai.12883.

**Childhood asthma and smoking exposures before conception - a three-generational cohort study.**

Bråbäck L<sup>1</sup>, Lodge CJ<sup>1,2,3</sup>, Lowe AJ<sup>1,2,3</sup>, Dharmage SC<sup>2,3</sup>, Olsson D<sup>1</sup>, Forsberg B<sup>1</sup>.

**BACKGROUND:**

Some human and animal studies have recently shown that maternal grandmother's smoking during pregnancy increases the risk of asthma in the grandchildren. We have investigated whether sex of the exposed parent and/or grandchild modifies the association between grandmaternal smoking and grandchild asthma.

**METHODS:**

We formed a cohort study based on linkage of national registries with prospectively collected data over three generations. Smoking habits in early pregnancy were registered since 1982 and purchases of prescribed medication since 2005. In all, 10329 children born since 2005 had information on maternal and grandmaternal smoking on both sides and were followed from birth up to 6 years of age. Ages when medication was purchased were used to classify the cohort into never, early transient (0-3 years), early persistent (0-3 and 4-6 years) and late-onset (4-6 years) phenotypes of childhood asthma.

**RESULTS:**

Maternal grandmother's smoking was associated with an increased odds of early persistent asthma after adjustment for maternal smoking and other confounders (odds ratio 1.29, 95% confidence interval 1.10-1.51). Grandchild sex did not modify the association. Paternal grandmother's smoking was not associated with any of the asthma phenotypes.

**CONCLUSION:**

Maternal but not paternal exposure to nicotine before conception was related to an increased risk of early persistent childhood asthma, but not other asthma phenotypes. Our findings are possibly consistent with a sex specific mode of epigenetic transfer.

**Vit D and Preeclampsia**

Taiwan J Obstet Gynecol. 2018 Apr;57(2):241-247. doi: 10.1016/j.tjog.2018.02.013.

**Association of vitamin D level and vitamin D deficiency with risk of preeclampsia: A systematic review and updated meta-analysis.**

Akbari S<sup>1</sup>, Khodadadi B<sup>2</sup>, Ahmadi SAY<sup>3</sup>, Abbaszadeh S<sup>4</sup>, Shahsavar F<sup>5</sup>.

*OBJECTIVES:*

Because of the immune modulatory effects of vitamin D3 in preeclampsia, we intend to have a systematic review and meta-analysis on association of both 25-hydroxy vitamin D (25-OHD) level (parametric approach) and 25-OHD deficiency (non-parametric approach) with preeclampsia. As well, for the parametric part, we used receiver operating characteristic (ROC) curve model.

*MATERIALS AND METHODS:*

We used Web of Science, PubMed and Science Direct data bases through searching in titles. Google Scholar search engine was used in order to find missing papers. Finally 23 studies were imported. Both random and fixed models were reported.

*RESULTS:*

Based on the forest plot, lower levels of 25-OHD were significantly associated with risk of preeclampsia (fixed and random  $P < 0.001$ ). Based on the forest plot, vitamin D deficiency (25-OHD  $< 20$  ng/ml) was significantly associated with risk of preeclampsia (fixed  $P < 0.0001$ ; random  $P = 0.0029$ ; fixed OR = 1.33; random OR = 1.54). Based on ROC curve results, we found 2 cutoffs of 10.60 and 20.05 ng/ml.

*CONCLUSION:*

Women with vitamin D deficiency at cutoff 20 ng/ml are more at risk of preeclampsia. This association can be specific up to 90% at 10.60 ng/ml cutoff. Treatment of vitamin D deficiency is necessary before pregnancy.

**Childhood sugar and cognition****Associations of Prenatal and Child Sugar Intake With Child Cognition**

Juliana F.W. Cohen, ScD Sheryl L. Rifas-Shiman, MPH Jessica Young, PhD Emily Oken, MPH, MD

DOI: <https://doi.org/10.1016/j.amepre.2018.02.020>

**Introduction**

Sugar consumption among Americans is above recommended limits, and excess sugar intake may influence cognition. The aim of this study was to examine associations of pregnancy and offspring sugar consumption (sucrose, fructose) with child cognition. Additionally, associations of maternal and child consumption of sugar-sweetened beverages (SSBs), other beverages (diet soda, juice), and fruit with child cognition were examined.

**Methods**

Among 1,234 mother–child pairs enrolled 1999–2002 in Project Viva, a pre-birth cohort, in 2017 diet was assessed during pregnancy and early childhood, and cognitive outcomes in early and mid-childhood (median ages 3.3 and 7.7 years). Analyses used linear regression models adjusted for maternal and child characteristics.

**Results**

Maternal sucrose consumption (mean 49.8 grams/day [SD=12.9]) was inversely associated with mid-childhood Kaufman Brief Intelligence Test (KBIT-II) non-verbal scores (–1.5 points per 15 grams/day, 95% CI= –2.8, –0.2). Additionally, maternal SSB consumption was inversely associated with mid-childhood cognition, and diet soda was inversely associated with early and mid-childhood cognition scores. Early childhood consumption of SSBs was inversely associated with mid-childhood KBIT-II verbal scores (–2.4 points per serving/day, 95% CI= –4.3, –0.5) while fruit consumption was associated with higher cognitive scores in early and mid-childhood. Maternal and child fructose and juice consumption were not associated with cognition. After adjusting for multiple comparisons, the association between maternal diet soda consumption and mid-childhood KBIT-II verbal scores remained significant.

**Conclusions**

Sugar consumption, especially from SSBs, during pregnancy and childhood, and maternal diet soda consumption may adversely impact child cognition, while child fruit consumption may lead to improvements. Interventions and policies that promote healthier diets may prevent adverse effects on childhood cognition.

**Coffee and Breast CA**

Cancer Causes &amp; Control pp 1–7

**Interactions of coffee consumption and postmenopausal hormone use in relation to breast cancer risk in UK Biobank**

Lusine Yaghjyan Shannan Rich Liang Mao Volker Mai Kathleen M. Egan

**Purpose**

We investigated the association of coffee consumption with postmenopausal breast cancer risk, overall and by the status of postmenopausal hormone therapy (PMH).

**Methods**

This study included 126,182 postmenopausal women (2,636 with breast cancer and 123,546 without) from UK Biobank. Cancer diagnoses were ascertained through the linkage to the UK National Health Service Central Registers. Information on breast cancer risk factors and coffee consumption was collected at baseline and updated during follow-up. We used Cox proportional hazards regression to evaluate associations between coffee consumption and breast cancer, overall and in stratified analyses by woman's PMH status (none, past, current).

**Results**

In the overall analysis, coffee consumption was not associated with breast cancer risk (Hazard Ratio [HR] 1.00, 95% CI 0.91–1.11 for 2–3 cups/day, and HR 0.98, 95% CI 0.87–1.10 for  $\geq 4$  cups/day,  $p$ -trend = 0.69). Women with no PMH history who consumed  $\geq 4$  cups/day had a 16% reduced risk of breast cancer as compared to women who consumed  $< 7$  cups/week (HR 0.84, 95% CI 0.71–1.00). Among women with past PMH, those consuming  $\geq 4$  cups/day had a 22% greater risk of breast cancer than women consuming  $< 7$  cups/week (HR 1.22, 95% CI 1.01–1.47). No association was found among current PMH users. We found no significant interaction between PMH and coffee consumption ( $p = 0.24$ ).

**Conclusions**

Coffee consumption might be associated with increased breast cancer risk in women who used hormones in the past. Further studies are warranted to confirm these findings and elucidate potential biological mechanisms underlying the observed associations.

## 8. VISCERA

### IDA and Celiac's disease

#### Prevalence of Celiac Disease in Patients with Iron Deficiency Anemia – a Systematic Review with Meta-analysis

Srihari Mahadev\* Monika Laszkowska\* Johan Sundström Magnus Björkholm ,  
Benjamin Lebwohl Peter HR. Green Jonas F. Ludvigsson

DOI: <https://doi.org/10.1053/j.gastro.2018.04.016>

#### Background & Aims

Anemia is common in patients with celiac disease and a frequent presentation. Guidelines recommend screening iron-deficient patients with anemia for celiac disease. However, the reported prevalence of celiac disease among patients with iron-deficiency anemia (IDA) varies. We performed a systematic review to determine the prevalence of biopsy-verified celiac disease in patients with IDA.

#### Methods

We performed a systematic review of manuscripts published in PubMed Medline or EMBASE through July 2017 for the term celiac disease combined with anemia or iron-deficiency. We used fixed-effects inverse variance-weighted models to measure the pooled prevalence of celiac disease. Meta-regression was used to assess subgroup heterogeneity.

#### Results

We identified 18 studies comprising 2998 patients with IDA for inclusion in our analysis. Studies originated from the United Kingdom, United States, Italy, Turkey, Iran, and Israel. The crude unweighted prevalence of celiac disease was 4.8% (n=143). Using a weighted pooled analysis, we demonstrated a prevalence of biopsy-confirmed celiac disease 3.2% (95% CI, 2.6%–3.9%) in patients with IDA. However, heterogeneity was high ( $I_2 = 67.7\%$ ). The prevalence of celiac disease was not significantly higher in studies with a mean participant age older or younger than years, nor in studies with a mixed-sex vs female-predominant ( $\geq 60\%$ ) population. On meta-regression, year of publication, the proportion of females, age at celiac disease testing, and the prevalence of in the general population were not associated with the prevalence of celiac disease in patients with IDA. In the 8 studies fulfilling all our quality criteria, the pooled prevalence of celiac disease was 5.5% (95% CI, 4.1%–6.9%).

#### Conclusions

In a systematic review and meta-analysis, we found that approximately 1 in 31 patients with IDA have histologic evidence of celiac disease. This prevalence value justifies the practice of testing patients with IDA for celiac disease.



**Diet and bowel inflammation**

Eur J Nutr. 2018 Apr 19. doi: 10.1007/s00394-018-1690-5.

**Association between the Dietary Inflammatory Index (DII) and urinary enterolignans and C-reactive protein from the National Health and Nutrition Examination Survey-2003-2008.**

Shivappa N<sup>1,2,3</sup>, Wirth MD<sup>4,5,6,7</sup>, Murphy EA<sup>8</sup>, Hurley TG<sup>4,5</sup>, Hébert JR<sup>4,5,7</sup>.

**BACKGROUND:**

Enterolignans are important biomarkers of microbiota diversity, with higher levels indicating greater diversity. Diet and inflammation have been shown to play a role in maintaining microbiota diversity. This study examined whether inflammatory potential of diet, as measured by the Dietary Inflammatory Index (DII<sup>®</sup>) has an impact on levels of urinary enterolignans in the National Health and Nutrition Examination Survey (NHANES) 2003-2008. We also carried out construct validation of the DII with C-reactive protein (CRP).

**METHODS:**

Data came from NHANES 2003-2008. Enterolignans [enterodiol (END) and enterolactone (ENL)] and CRP were assayed from urine and serum specimens, respectively. Energy-adjusted DII (E-DII) scores were calculated from food intakes assessed using 24-h dietary recalls and expressed per 1000 calories consumed. Associations were examined using survey-based multivariable linear and logistic regression for enterolignans, and logistic regression for CRP.

**RESULTS:**

After multivariable adjustment, higher E-DII scores (i.e., indicating a relatively more pro-inflammatory diet) were associated with lower levels of creatinine-normalized END [beta coefficient (b)<sub>DIIquartile4vs1</sub> = - 1.22; 95% CI = - 0.69, - 1.74; P<sub>trend</sub> ≤ 0.001] and ENL (b<sub>DIIquartile4vs1</sub> = - 7.80; 95% CI = - 5.33, - 10.26; P<sub>trend</sub> ≤ 0.001). A positive association was also observed when enterolignans were dichotomized based on the cut-off of the 75th percentile value. In this same sample, the E-DII also was associated with CRP ≥ 3 mg/l (OR<sub>DIIcontinuous</sub> = 1.12; 95% CI 1.05, 1.19).

**CONCLUSION:**

In these NHANES data, there was an association between E-DII score and enterolignans. This study also provided construct validation of the E-DII using CRP in a nationally representative sample. The results indicate that dietary inflammatory potential is associated with urinary enterolignans, a potential marker for microbiota diversity. However, studies are required to understand the direct association between DII and microbiota.

**Probiotics helps depression**

Ann Gen Psychiatry. 2017; 16: 14. . doi: 10.1186/s12991-017-0138-2 PMCID: PMC5319175  
PMID: 28239408

**The effects of probiotics on depressive symptoms in humans: a systematic review**

Caroline J. K. Wallace<sup>✉</sup> and Roumen Milev

It has been reported that gut probiotics play a major role in the bidirectional communication between the gut and the brain.

Probiotics may be essential to people with depression, which remains a global health challenge, as depression is a metabolic brain disorder. However, the efficacy of probiotics for depression is controversial.

This study aimed to systematically review the existing evidence on the effect of probiotics-based interventions on depression. Randomized, controlled trials, identified through screening multiple databases and grey literature, were included in the meta-analysis. The meta-analysis was performed using Review Manager 5.3 software using a fixed-effects model. The meta-analysis showed that probiotics significantly decreased the depression scale score (MD (depressive disorder) = -0.30, 95% CI (-0.51--0.09),  $p = 0.005$ ) in the subjects. Probiotics had an effect on both the healthy population (MD = -0.25, 95% CI (-0.47--0.03),  $p = 0.03$ ) and patients with major depressive disorder (MDD) (MD = -0.73, 95% CI (-1.37--0.09),  $p = 0.03$ ). Probiotics had an effect on the population aged under 60 (MD = -0.43, 95% CI (-0.72--0.13),  $p = 0.005$ ), while it had no effect on people aged over 65 (MD = -0.18, 95% CI (-0.47-0.11),  $p = 0.22$ ).

This is the first systematic review and meta-analysis with the goal of determining the effect of probiotics on depression. We found that probiotics were associated with a significant reduction in depression, underscoring the need for additional research on this potential preventive strategy for depression.

**IBS and SI pain**

Arthritis Care Res (Hoboken). 2017 Jul 21. doi: 10.1002/acr.23323.

**Prevalence of Sacroiliitis in Inflammatory Bowel Disease Using a Standardized Computed Tomography Scoring System.**

Chan J<sup>1</sup>, Sari I<sup>2</sup>, Salonen D<sup>3</sup>, Silverberg MS<sup>4</sup>, Haroon N<sup>5</sup>, Inman RD<sup>5</sup>.

*OBJECTIVE:*

There is an increasing emphasis on the early identification and treatment of ankylosing spondylitis (AS) of which the hallmark is sacroiliitis. Patients with inflammatory bowel disease (IBD) are at increased risk of AS and often receive computed tomography (CT) scans of their abdomen, affording clinicians the opportunity to determine the presence of sacroiliitis. Previous studies using CT have relied only on the radiologist's gestalt or a nonvalidated adaptation of the modified New York criteria. Our aim is to assess the prevalence of sacroiliitis in IBD using a validated screening tool and to determine how frequently these patients are referred for rheumatologic evaluation.

*METHODS:*

Patients with IBD were recruited from an IBD clinic. Control patients were recruited from a urology clinic and were confirmed to be without back pain, spondylitis, psoriasis, colitis, or uveitis by chart review. CT scans were read by 2 blinded readers and sacroiliitis was defined by the presence of ankylosis or a total erosion score of  $\geq 3$ .

*RESULTS:*

CT scans were available in 233 Crohn's disease (CD) patients, 83 ulcerative colitis (UC) patients, and 108 control patients, and sacroiliitis was seen in 15%, 16.9%, and 5.6% of patients, respectively. The prevalence was higher in patients with IBD than in controls ( $P = 0.007$ ), with no significant difference between CD and UC patients. Of the 49 IBD patients found to have sacroiliitis by CT scan, only 5 had been referred to a rheumatologist.

*CONCLUSION:*

There is a 3-fold higher prevalence of sacroiliitis in IBD compared with controls. Despite a growing awareness of this increased prevalence, many patients are not referred to a rheumatologist.

**13 C. AIRWAYS/SWALLOWING/SPEECH****Sleep apnea****Sleep Medicine****Relationship between obstructive sleep apnoea syndrome and essential hypertension: a dose–response meta-analysis**

WanyuanXia<sup>a</sup>YanhongHuang<sup>b</sup>BinPeng<sup>a</sup>XinZhang<sup>a</sup>QingmengWu<sup>a</sup>YiyingSang<sup>a</sup>YetaoLuo<sup>a</sup>XunLiu<sup>a</sup>  
QianChen<sup>a</sup>KaocongTian<sup>a</sup>  
<https://doi.org/10.1016/j.sleep.2018.03.016>

**Highlights** of “Relationship between obstructive sleep apnoea syndrome and essential hypertension: a dose-response meta-analysis”

- Assessed OSAS in relation to essential hypertension occurrence risk.
- Examined dose–response association between OSAS and essential hypertension.
- Explored the association between OSAS and hypertension in the light of prevention.

**Abstract****Objective**

The objective of this study was to summarize the evidence regarding the relationship between obstructive sleep apnoea syndrome (OSAS) and the risk of essential hypertension.

**Methods**

The study was a dose–response meta-analysis of observational studies. The PubMed, Embase, CNKI, VIP and CBM databases were searched to collect relative studies examining the relationship between OSAS and the risk of essential hypertension. Studies were retrieved from database establishment through September 2016, and new literature published between September 2016 and May 2017 was later supplemented. Linear and non-linear dose–response models were used to assess the relationship between apnoea–hypopnea index (AHI), which was used to reflect the severity of OSAS, and the risk of essential hypertension. Stata 13.0 was used for the meta-analysis.

**Results**

Six prospective cohort studies and one case–control study were included, for a total sample size of 6098. The dose–response meta-analysis showed that a high AHI significantly increased the risk of essential hypertension compared with a low AHI (odds ratio (OR) = 1.77, 95% confidence interval (CI) (1.30, 2.41),  $p = 0.001$ ). The linear dose–response meta-analysis showed that the risk of essential hypertension increased by 17% for every 10 events/h increase in the AHI (OR = 1.17, 95% CI (1.07, 1.27),  $p = 0.001$ ), and the results of the non-linear dose–response meta-analysis showed that the risk of essential hypertension increased with increasing AHI value.

**Conclusion**

A potential dose–response relationship exists between the severity of OSAS and the risk of essential hypertension. This relationship should be considered when developing prevention measures for essential hypertension.

**Bedroom environment and sleep apnea**

J Clin Sleep Med. 2018 Mar 30. pii: jc-17-00342.

**Effects of Bedroom Environmental Conditions on the Severity of Obstructive Sleep Apnea.**

Lappharat S, Taneepanichskul N, Reutrakul S, Chirakalwasan N.

## Abstract

*STUDY OBJECTIVES:*

Epidemiological associations have demonstrated the effects of long-term air pollution to obstructive sleep apnea (OSA) through a physiological mechanism linking particulate matter exposure to OSA. This study aimed to determine the relationship between bedroom environmental conditions, OSA severity, and sleep quality.

*METHODS:*

Sixty-three participants were enrolled for an overnight polysomnography; OSA was diagnosed between May to August 2016. Personal characteristics and sleep quality were obtained by a face-to-face interview. Bedroom environments, including data on particulate matter with an aerodynamic diameter less than 10  $\mu\text{m}$  (PM10), temperature, and relative humidity, were collected by personal air sampling and a HOBO tempt/RH data logger.

*RESULTS:*

Sixty-eight percent of the participants experienced poor sleep. An elevation in 1-year mean PM10 concentration was significantly associated with an increase in apnea-hypopnea index (beta = 1.04,  $P = .021$ ) and respiratory disturbance index (beta = 1.07,  $P = .013$ ). An increase of bedroom temperature during sleep was significantly associated with poorer sleep quality (adjusted odds ratio 1.46, 95% confidence interval 1.01-2.10,  $P = .044$ ). Associations between PM10 concentration and respiratory disturbance index were observed in the dry season (beta = 0.59,  $P = .040$ ) but not in the wet season (beta = 0.39,  $P = .215$ ). PM10 was not associated with subjective sleep quality.

*CONCLUSIONS:*

Elevation of PM10 concentration is significantly associated with increased OSA severity. Our findings suggest that reduction in exposure to particulate matter and suitable bedroom environments may lessen the severity of OSA and promote good sleep.

**Heart function and sleep apnea**

Sleep Breath. 2018 Apr 10. doi: 10.1007/s11325-018-1652-4.

**Cycle length identifies obstructive sleep apnea and central sleep apnea in heart failure with reduced ejection fraction.**

Bitter T<sup>1</sup>, Özdemir B<sup>2</sup>, Fox H<sup>2</sup>, Horstkotte D<sup>2</sup>, Oldenburg O<sup>2</sup>.

*AIM:*

To clarify whether unmasking of central sleep apnea during continuous positive airway pressure (CPAP) initiation can be identified from initial diagnostic polysomnography (PSG) in patients with heart failure with reduced ejection fraction (HFREF) and obstructive sleep apnea (OSA)

**MATERIALS AND METHODS:** Forty-three consecutive patients with obstructive sleep apnea and central sleep apnea (OSA/CSA) in HFREF were matched with 43 HFREF patients with OSA and successful CPAP initiation. Obstructive apneas during diagnostic PSG were then analyzed for cycle length (CL), ventilation length (VL), apnea length (AL), time to peak ventilation (TTPV), and circulatory delay (CD). We calculated duty ratio (DR) as the ratio of VL/CL and mathematic loop gain (LG).

*RESULTS:*

While AL was similar, CL, VL, TTPV, CD, and DR was significantly longer in patients with OSA/CSA compared to those with OSA, and LG was significantly higher. Receiver operator curves identified optimal cutoff values of 50.2 s for CL (area under the curve (AUC) 0.85, 29.2 s for VL (AUC 0.92), 11.5 s for TTPV (AUC 0.82), 26.4 s for CD (AUC 0.79), and 3.96 (AUC 0.78)) respectively for LG to identify OSA/CSA.

*CONCLUSION:*

OSA/CSA in HFREF can be identified by longer CL, VL, TTPV, and CD from obstructive events in initial diagnostic PSG. The underlying mechanisms seem to be the presence of an increased LG.

## CPAP and erectile dysfunction

**Sleep Medicine**  
**Original Article****CPAP therapy improves erectile function in patients with severe obstructive sleep apnea**

IRichardSchulz<sup>ab</sup>FabianBischoff<sup>c</sup>WolfgangGaletke<sup>d</sup>HenningGall<sup>b</sup>JörgHeitmann<sup>b</sup>AndreaHetzenecker<sup>c</sup>MarkusLaudenburg<sup>d</sup>TillJonasMagnus<sup>b</sup>GeorgNilius<sup>c</sup>ChristinaPriegnitz<sup>f</sup>WinfriedRanderath<sup>f</sup>MaikSchröder<sup>e</sup>MarcelTremel<sup>f</sup>MichaelArzt<sup>c</sup>German Sleep Apnea Research Network (GERSAN)

<https://doi.org/10.1016/j.sleep.2018.03.018>Get rights and content

**Highlights**

- Erectile dysfunction is very prevalent in patients with severe sleep apnea.
- CPAP therapy improves erectile function in most seriously affected patients.
- Improvements of erectile function under CPAP may depend on therapeutic compliance.
- The benefits of CPAP on erectile function are linked to better quality of life.
- Randomized controlled trials are needed to confirm these findings.

**Objectives**

Erectile dysfunction (ED) is highly prevalent in obstructive sleep apnea (OSA), however, the effect of continuous positive airway pressure (CPAP) therapy on erectile function has not yet been thoroughly investigated in these patients.

**Methods**

Ninety-four men with severe OSA (ie with an apnea-hypopnea-index  $\geq 30$ /h of sleep) were prospectively evaluated for the presence and severity of ED before and after 6-12 months of CPAP therapy. The abbreviated version of the International Index of Erectile Function, ie the IIEF-5, was used to rate erectile function. Furthermore, all study participants responded to standard questionnaires of daytime sleepiness (Epworth Sleepiness Scale), quality of life (WHO Wellbeing 5 questionnaire) and depression (Major Depression Inventory).

**Results**

ED as defined by an IIEF-5 score of  $\leq 21$  was present in 64 patients (ie 68.1%). CPAP treatment significantly improved erectile function in those patients suffering from moderate and severe ED. Additionally, a trend for a correlation between the improvement of erectile function under CPAP and the hours of its use was observed. Finally, this effect was associated with larger improvements of quality of life in affected patients.

**Conclusions**

ED is very frequent in men with severe OSA and can at least partly be reversed by long-term CPAP therapy in most seriously affected patients. The beneficial effect on erectile function may depend on CPAP compliance and is accompanied by improvements of quality of life. Randomized controlled trials are needed to confirm these findings.

## Stroke and CPAP

### **Role of positive airway pressure therapy for obstructive sleep apnea in patients with stroke: A randomized controlled trial**

Journal of Clinical Sleep Medicine — | April 18, 2018

Gupta A, et al.

This study examined how continuous positive airway pressure (CPAP) treatment effects the prevention of new vascular events among patients with stroke and obstructive sleep apnea (OSA). Patients with stroke and OSA who used CPAP treatment had significantly better stroke outcomes and statistically nonsignificant favorable outcomes regarding recurrence of vascular events.

#### **Methods**

- The study cohort consisted of consecutive conscious patients presenting with first imaging-confirmed arterial stroke, 6 weeks or more after ictus.
- Enrollees underwent clinical and polysomnography (PSG) testing.
- Patients with an apnea-hypopnea index (AHI) of more than 15 events/hour were randomized between posttitration nightly CPAP treatment and non-CPAP (received best medical treatment) groups.
- Researchers assessed any new vascular events found at 3, 6, and 12 months follow-up from randomization as the primary outcome measure, and for the secondary outcome, clinical stroke outcomes (using the Barthel Index and modified Rankin scale) and neuropsychological parameters.

#### **Results**

- Out of the 679 patients with stroke who were screened, 116 reported for PSG, 83 had AHI > 15 events/hour, and 70 (34 in CPAP and 36 in non-CPAP) were randomized.
- During this research, 4 patients crossed over from the CPAP to the non-CPAP group.
- Both groups had similar age (mean age  $53.41 \pm 9.85$  in CPAP vs  $52.69 \pm 13.23$  years in non-CPAP,  $P=.81$ ) and sex distribution (24 males in CPAP vs 33 males in non-CPAP,  $P=.79$ ).
- One vascular event was seen at 12-month follow-up (3.33%) in the CPAP group and in the non-CPAP group ( $P=.23$ ) 6 events (15%) were reported.
- Significantly more patients in the CPAP group compared to the non-CPAP group (53% vs 27%) experienced modified Rankin scale score improvement  $\geq 1$  at 12-month follow-up.

Sleep and cognitive decline



Ann Neurol. 2018 Mar;83(3):472-482. doi: 10.1002/ana.25166. Epub 2018 Mar 3.

**Sleep and cognitive decline: A prospective nondemented elderly cohort study.**

Suh SW<sup>1</sup>, Han JW<sup>1</sup>, Lee JR<sup>1</sup>, Byun S<sup>1</sup>, Kwon SJ<sup>1</sup>, Oh SH<sup>1</sup>, Lee KH<sup>1</sup>, Han G<sup>1</sup>, Hong JW<sup>1</sup>, Kwak KP<sup>2</sup>, Kim BJ<sup>3</sup>, Kim SG<sup>4</sup>, Kim JL<sup>5</sup>, Kim TH<sup>6</sup>, Ryu SH<sup>7</sup>, Moon SW<sup>8</sup>, Park JH<sup>9</sup>, Seo J<sup>10</sup>, Youn JC<sup>11</sup>, Lee DY<sup>12,13</sup>, Lee DW<sup>14</sup>, Lee SB<sup>15</sup>, Lee JJ<sup>15</sup>, Jhoo JH<sup>16</sup>, Kim KW<sup>1,13,17,18</sup>.

**OBJECTIVE:**

To investigate sleep disturbances that induce cognitive changes over 4 years in nondemented elderlies.

**METHODS:**

Data were acquired from a nationwide, population-based, prospective cohort of Korean elderlies (2,238 normal cognition [NC] and 655 mild cognitive impairment [MCI]). At baseline and 4-year follow-up assessments, sleep-related parameters (midsleep time, sleep duration, sleep latency, subjective sleep quality, sleep efficiency, and daytime dysfunction) and cognitive status were measured using the Pittsburgh Sleep Quality Index and Consortium to Establish a Registry for Alzheimer's Disease Assessment, respectively. We used logistic regression models adjusted for covariates including age, sex, education, apolipoprotein E genotype, Geriatric Depression Scale, Cumulative Illness Rating Scale, and physical activity.

**RESULTS:**

In participants with NC, long sleep latency (>30 minutes), long sleep duration ( $\geq 7.95$  hours), and late midsleep time (after 3:00 am) at baseline were related to the risk of cognitive decline at 4-year follow-up assessment; odds ratio (OR) was 1.40 for long sleep latency, 1.67 for long sleep duration, and 0.61 for late midsleep time. These relationships remained significant when these variables maintained their status throughout the follow-up period. Newly developed long sleep latency also doubled the risk of cognitive decline. In those with MCI, however, only long sleep latency reduced the chance of reversion to NC (OR = 0.69).

**INTERPRETATION:**

As early markers of cognitive decline, long sleep latency can be used for elderlies with NC or MCI, whereas long sleep duration and relatively early sleep time might be used for cognitively normal elderlies only. Ann Neurol 2018;83:472-482.

## 14. HEADACHES

### Comparison of tension and migraine

Pain. 2018 Apr;159(4):793-803. doi: 10.1097/j.pain.0000000000001151.

#### **Comparison of somatosensory cortex excitability between migraine and "strict-criteria" tension-type headache: a magnetoencephalographic study.**

Chen WT<sup>1,2,3,4</sup>, Hsiao FJ<sup>1</sup>, Ko YC<sup>3,5</sup>, Liu HY<sup>2,3,4</sup>, Wang PN<sup>1,3,4</sup>, Fuh JL<sup>1,3,4</sup>, Lin YY<sup>1,2,3,4</sup>, Wang SJ<sup>1,2,3,4</sup>.

Tension-type headache (TTH) and migraine are both common types of headaches. Despite distinct symptoms, TTH and migraine are highly comorbid and exhibit many clinical similarities.

This study enrolled consecutive patients with TTH and age- and sex-matched patients with migraine and healthy controls to investigate whether TTH and migraine are similar in brain excitability change assessed by magnetoencephalography. Patients with TTH were excluded if they reported any headache features or associated symptoms of migraine. In response to paired-pulse electrical stimulations, the gating responses obtained from the contralateral primary somatosensory cortex differed between groups.

The first response, which reflected the preactivation excitability, was smaller in the migraine group ( $29.54 \pm 2.31$  pAm) compared with the TTH group ( $79.76 \pm 8.36$ ,  $P < 0.001$ ) and controls ( $59.95 \pm 4.26$ ,  $P = 0.006$ ). The gating ratio (ie, the ratio of the second vs first response strength) was  $0.76 \pm 0.03$  in controls,  $0.88 \pm 0.03$  in the migraine group,  $0.93 \pm 0.03$  in the TTH group, with a significant increase in TTH ( $P = 0.003$  vs controls) suggesting central disinhibition. The area under the receiver operating characteristic curve of the first response strength in differentiating between TTH and migraine was  $0.85 \pm 0.44$ , indicating excellent discrimination. In conclusion, TTH and migraine are different clinical entities in view of somatosensory cortex excitability.

The preactivation excitability assessed through somatosensory gating is a potential marker for differentiating between TTH and migraine.

PMID: 29319611 DOI: 10.1097/j.pain.0000000000001151

**32 A. KNEE/ACL****Anterolateral ligaments****Incidence of Anterolateral Ligament Tears in the Anterior Cruciate Ligament-Deficient Knee: A Magnetic Resonance Imaging Analysis**

CAPT Christopher Gauder, M.D. LT COL Scot Campbell, M.D. MAJ Michael Sciortino, P.A.-C. ,  
LT COL Mark Slabaugh, M.D.  
DOI: <https://doi.org/10.1016/j.arthro.2018.01.057>

**Purpose**

The purpose of this study is to determine the incidence of anterolateral ligament (ALL) tears on magnetic resonance imaging (MRI) in patients diagnosed with anterior cruciate ligament (ACL) tears. Furthermore, this study sought to determine the inter- and intraobserver reliability in diagnosing an ALL tear.

**Methods**

The MRI radiologic database at a community military hospital was queried for ACL tears over the period of January 2011 to April 2015. During this time, 181 MRIs were identified as having ACL tears. The MRIs were then independently reviewed by an orthopaedic surgeon and a musculoskeletal (MSK) trained radiologist. Both reviewers, independently confirmed the ACL tears, and the ALL was noted to be either torn, intact, or not visualized on axial, sagittal, and coronal images. Four weeks later the same MRIs were then reviewed for the presence and location of an ALL tear to determine inter- and intraobserver reliability.

**Results**

The MSK radiologist found ALL tears on MRI in 28.2% of the cases, while the orthopaedic surgeon found ALL tears in 39.8% of the cases; 5.5% of the MRIs were characterized as having a nonvisualized ALL. The interobserver reliability was noted to have a kappa value of 0.333. The intraobserver reliability of the MSK radiologist and orthopaedic surgeon demonstrated a kappa value of 0.654 and 0.251, respectively.

**Conclusions**

This study shows that the majority of patients with a known ACL tear on MRI do not have a tear of the ALL. Additionally, the interobserver reliability of surgeons and radiologist is fair. In this study, the MSK radiologist had higher intraobserver reliability when looking for an ALL tear.

**37. OSTEOARTHRITIS/KNEE****PRP and HA**

Clin Rheumatol. 2018 May;37(5):1341-1350. doi: 10.1007/s10067-018-3985-6. Epub 2018 Jan 31.

**Comparison of hyaluronic acid and PRP intra-articular injection with combined intra-articular and intraosseous PRP injections to treat patients with knee osteoarthritis.**

Su K<sup>1</sup>, Bai Y<sup>2</sup>, Wang J<sup>2</sup>, Zhang H<sup>2</sup>, Liu H<sup>3</sup>, Ma S<sup>2</sup>.

The aim of this study was to evaluate the benefit provided by intraosseous infiltration combined with intra-articular injection of platelet-rich plasma to treat mild and moderate stages of knee joint degeneration (Kellgren-Lawrence score II-III) compared with other treatments, specifically intra-articular injection of PRP and of HA.

Eighty-six patients with grade II to grade III knee OA according to the Kellgren-Lawrence classification were randomly assigned to intra-articular combined with intraosseous injection of PRP (group A), intra-articular PRP (group B), or intra-articular HA (group C). Patients in group A received intra-articular combined with intraosseous injection of PRP (administered twice, 2 weeks apart). Patients in group B received intra-articular injection of PRP every 14 days. Patients in group C received a series of five intra-articular injections of HA every 7 days. All patients were evaluated using the Visual Analogue Scale (VAS) and Western Ontario and McMaster Universities (WOMAC) score before the treatment and at 1, 3, 6, 12, and 18 months after treatment. There were significant improvements at the end of the 1st month. Notably, group A patients had significantly superior VAS and WOMAC scores than were observed in groups B and C. The VAS scores were similar in groups B and group C after the 6th month. Regarding the WOMAC scores, groups B and C differed at the 1st, 3rd, 6th, and 12th months; however, no significant difference was observed at the 18th month.

The combination of intraosseous with intra-articular injections of PRP resulted in a significantly superior clinical outcome, with sustained lower VAS and WOMAC scores and improvement in quality of life within 18 months.

## Exercise helps

**Physical Activity and Exercise Therapy Benefits More Than Just Symptoms and Impairments in People With Hip and Knee Osteoarthritis**

**Authors:** Søren T. Skou, PT, PhD<sup>1,2</sup>, Bente Klarlund Pedersen, MD, DMSc<sup>3</sup>, J. Haxby Abbott, PhD, DPT, FNZCP<sup>4</sup>, Brooke Patterson, PT<sup>5</sup>, Christian Barton, PT, PhD<sup>5</sup>

**Published:** *Journal of Orthopaedic & Sports Physical Therapy*,  
2018 **Volume:**0 **Issue:**0 **Pages:**1–36 **DOI:**10.2519/jospt.2018.7877

**Synopsis**

Hip and knee osteoarthritis (OA) are among the leading causes of global disability, highlighting the need for early, targeted, and effective treatments.

The benefits on symptoms and impairments of exercise therapy in people with hip and knee OA are substantial and supported by high-quality evidence, underlining that it should be part of first line treatment offered to all people with hip and knee OA in clinical practice. Furthermore, unlike other treatments for OA such as analgesia and surgery, exercise therapy is not associated with risk of serious harm. Promoting and helping people with OA become more physically active alongside participating in structured exercise therapy targeting symptoms and impairments is crucial considering the majority of people with hip and knee OA do not meet physical activity recommendations. OA is associated with a range of chronic comorbidities, including type 2 diabetes, cardiovascular disease, and dementia, all of which are associated with chronic low-grade inflammation. Physical activity and exercise therapy not only improves symptoms and impairments of OA, it is also effective as prevention of at least 35 chronic conditions and as treatment of at least 26 chronic conditions with one of the potential working mechanisms being exercise induced anti-inflammatory effects.

Patient education may be crucial to ensure long-term adherence and sustained positive effects on symptoms, impairments, physical activity levels and comorbidities. *J Orthop Sports Phys Ther, Epub 18 Apr 2018. doi:10.2519/jospt.2018.7877*

**59. PAIN****Psychological factors in pain**

BMJ Open. 2018 Apr 13;8(4):e020703. doi: 10.1136/bmjopen-2017-020703.

**The role of psychological factors in the perpetuation of pain intensity and disability in people with chronic shoulder pain: a systematic review.**

Martinez-Calderon J<sup>1,2</sup>, Meeus M<sup>2,3,4</sup>, Struyf F<sup>2</sup>, Miguel Morales-Asencio J<sup>5</sup>, Gijon-Nogueron G<sup>6</sup>, Luque-Suarez A<sup>1</sup>.

*INTRODUCTION:*

Chronic shoulder pain is a very complex syndrome, and the mechanisms involved in its perpetuation remain unclear. Psychological factors appear to play a role in the perpetuation of symptoms in people with shoulder chronicity. The purpose of this systematic review is to examine the role of psychological factors in the perpetuation of symptoms (pain intensity and disability) in people with chronic shoulder pain.

*METHODS AND ANALYSIS:*

A systematic search was performed on PubMed, AMED, CINAHL, PubPsych and EMBASE from inception to July 2017. Longitudinal studies with quantitative designs analysing the role of psychological factors on pain intensity, disability or both were included. The methodological quality of the included studies was evaluated with an adapted version of the Newcastle Ottawa Scale. The level of evidence per outcome was examined using the Grading of Recommendations Assessment, Development and Evaluation approach.

*RESULTS:*

A total of 27 articles were included with a sample of 11 176 people with chronic shoulder pain. The risk of bias ranges from 7/21 to 13/21 across the studies. The quality of the evidence was very low. High levels of self-efficacy, resilience and expectations of recovery were significantly associated with low levels of pain intensity and disability. Inversely, high levels of emotional distress, depressive symptoms, anxiety, preoperative concerns, fear-avoidance beliefs, somatisation and pain catastrophising were significantly associated with high levels of pain intensity and disability.

*DISCUSSION:*

Our results suggest that psychological factors may influence the perpetuation of pain intensity and disability, with very low evidence. A meta-analysis was not carried out due to the heterogeneity of the included studies so results should be interpreted with caution.

## Inflammation and cognitive function

Journal of Psychiatric Research

**Inflammatory markers and their possible effects on cognitive function in women with posttraumatic stress disorder**

- Risa Imai<sup>a</sup>, Hiroaki Hori<sup>b, ·</sup>, Mariko Itoh<sup>b</sup>, Toshiko Kamo<sup>e</sup>,  
**Show more**  
<https://doi.org/10.1016/j.jpsychires.2018.04.009>

**Highlights**

- We examined inflammatory markers and their relation to cognition in PTSD patients.
  - Serum IL-6 levels were significantly higher in PTSD patients than in controls.
    - IL-6 levels were not associated with comorbid MDD or childhood maltreatment.
    - Patients showed significantly lower performance on memory, language and attention.
      - Higher IL-6 levels in patients were associated with even lower cognitive function.

**Abstract**

Posttraumatic stress disorder (PTSD) has been associated with increased inflammation, albeit with some controversy. Another key feature of PTSD is compromised function in wide-ranging cognitive domains. Increased peripheral inflammation can contribute to cognitive dysfunction, although this relationship has not been studied in patients with PTSD.

Here, we examined blood inflammatory markers in adult patients with PTSD compared to healthy controls taking account of potentially confounding effects of childhood maltreatment and comorbid major depressive disorder (MDD), and explored the association between inflammation and cognition. We enrolled 40 women with PTSD, most of whom developed the disorder after interpersonal violence during adulthood, and 65 healthy control women. Diagnoses were made based on DSM-IV. History of childhood maltreatment was assessed using the Childhood Trauma Questionnaire (CTQ). Cognitive function was assessed using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Blood samples were collected for the measurement of 5 inflammatory markers including interleukin-6 (IL-6), soluble IL-6 receptor, interleukin-1 $\beta$ , high-sensitivity tumor necrosis factor- $\alpha$ , and high-sensitivity C-reactive protein. Compared to controls, patients with PTSD showed significantly higher IL-6 levels ( $p = 0.009$ ) and lower scores on all RBANS domains (all  $p < 0.01$ ). IL-6 levels in patients were not significantly associated with the presence/absence of comorbid MDD or CTQ scores. IL-6 levels in patients were significantly negatively correlated with RBANS visuospatial construction ( $p = 0.046$ ), language ( $p = 0.008$ ), attention ( $p = 0.036$ ) and total score ( $p = 0.008$ ).

These results suggest that elevated IL-6 is associated with PTSD and that the lower cognitive function in PTSD may be due at least partly to increased inflammation.

**CBT and chronic pain**

Pain. 2018 Apr;159(4):644-655. doi: 10.1097/j.pain.0000000000001150.

**Computerised training improves cognitive performance in chronic pain: a participant-blinded randomised active-controlled trial with remote supervision.**

Baker KS<sup>1,2</sup>, Georgiou-Karistianis N<sup>2</sup>, Lampit A<sup>3,4</sup>, Valenzuela M<sup>3</sup>, Gibson SJ<sup>1,5</sup>, Giummarra MJ<sup>1,6,7</sup>.

Chronic pain is associated with reduced efficiency of cognitive performance, and few studies have investigated methods of remediation.

We trialled a computerised cognitive training protocol to determine whether it could attenuate cognitive difficulties in a chronic pain sample. Thirty-nine adults with chronic pain (mean age = 43.3, 61.5% females) were randomised to an 8-week online course (3 sessions/week from home) of game-like cognitive training exercises, or an active control involving watching documentary videos. Participants received weekly supervision by video call. Primary outcomes were a global neurocognitive composite (tests of attention, speed, and executive function) and self-reported cognition. Secondary outcomes were pain (intensity; interference), mood symptoms (depression; anxiety), and coping with pain (catastrophising; self-efficacy). Thirty participants (15 training and 15 control) completed the trial. Mixed model intention-to-treat analyses revealed significant effects of training on the global neurocognitive composite (net effect size [ES] = 0.43, P = 0.017), driven by improved executive function performance (attention switching and working memory). The control group reported improvement in pain intensity (net ES = 0.65, P = 0.022). Both groups reported subjective improvements in cognition (ES = 0.28, P = 0.033) and catastrophising (ES = 0.55, P = 0.006).

Depression, anxiety, self-efficacy, and pain interference showed no change in either group. This study provides preliminary evidence that supervised cognitive training may be a viable method for enhancing cognitive skills in persons with chronic pain, but transfer to functional and clinical outcomes remains to be demonstrated. Active control results suggest that activities perceived as relaxing or enjoyable contribute to improved perception of well-being. Weekly contact was pivotal to successful program completion.



**Childhood experience and chronic pain**

Clin J Pain. 2018 May;34(5):402-408. doi: 10.1097/AJP.0000000000000549.

**The Incidence of Adverse Childhood Experiences (ACEs) and Their Association With Pain-related and Psychosocial Impairment in Youth With Chronic Pain.**

Nelson S<sup>1,2</sup>, Simons LE<sup>3</sup>, Logan D<sup>1,2</sup>.

*OBJECTIVES:*

Adverse childhood experiences (ACEs) in youth have been found to be frequently associated with several chronic illnesses, including chronic pain. However, this relationship remains poorly understood. Previous research has examined the association between ACEs and chronic pain, but these have primarily been examined in the context of adults with limited assessment of ACEs and individual pain conditions. The primary objectives of this study were to examine the incidence and psychological/pain-related correlates of ACEs in a sample of youth with chronic pain. Exploratory analyses were also examined using primary pain diagnosis and number of pain locations.

*METHODS:*

Data were gathered using retrospective data from a clinical databank. Participants were 141 youth aged 9 to 19 with chronic pain who presented for evaluation at a multidisciplinary pain clinic. Information on ACEs exposure, pain diagnostic information, pain-related impairment, and psychosocial functioning were gathered via self-report and retrospective review of the medical record.

*RESULTS:*

Results revealed that over 80% of youth with chronic pain reported at least 1 ACE in their lifetime. Further, multiple and univariate analyses of variance revealed that ACEs exposure is significantly associated with greater symptoms of anxiety, depression, and fear of pain, with  $\geq 3$  ACEs associated with greatest impairment in functioning. No relationships were found between ACEs and increased pain-related disability or pain intensity.

*DISCUSSION:*

ACEs exposure in youth with chronic pain occurs frequently and can be associated with increased psychosocial but not functional impairment. Future research is needed to further examine the relationship between ACEs and chronic pain in youth in a prospective manner.