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1. LUMBAR SPINE

Biochemical changes in LBP


Neurochemical changes in patients with chronic low back pain detected by proton magnetic resonance spectroscopy: A systematic review.
Zhao X¹, Xu M¹, Jorgenson K², Kong J².

BACKGROUND:
Low back pain is a highly prevalent health problem around the world, affecting 50% to 85% of people at some point in life. The purpose of this systematic review is to summarize the previous proton magnetic resonance spectroscopy studies on brain chemical changes in patients with chronic low back pain (CLBP).

METHODS:
We identified relevant studies from a literature search of PubMed and EMBASE from 1980 to March 2016. Data extraction was performed on the subjects' characteristics, MRS methods, spectral analyses, cerebral metabolites and perceptual measurements.

RESULTS:
The review identified 9 studies that met the inclusion criteria, comprised of data on 135 CLBP subjects and 137 healthy controls. Seven of these studies reported statistically different neurochemical alterations in patients with CLBP. The results showed that compared to controls, CLBP patients showed reductions of 1) N-acetyl-aspartate (NAA) in the dorsolateral prefrontal cortex (DLPFC), right primary motor cortex, left somatosensory cortex (SSC), left anterior insula and anterior cingulate cortex (ACC); 2) glutamate in the ACC; 3) myo-inositol in the ACC and thalamus; 4) choline in the right SSC; and 5) glucose in the DLPFC.

CONCLUSION:
This review provides evidence for alterations in the biochemical profile of the brain in patients with CLBP, which suggests that biochemical changes may play a significant role in the development and pathophysiology of CLBP and shed light on the development of new treatments for CLBP.
Smoking negative impact

The effect of smoking on clinical and structural damage in patients with axial spondyloarthritis: a systematic literature review

Virginia Villaverde-García Tatiana Cobo-Ibáñez Gloria Candelas-Rodríguez Daniel Seoane-Mato, Petra Díaz del Campo-Fontecha Mercedes Guerra Santiago Muñoz-Fernández Juan D Cañete

DOI: http://dx.doi.org/10.1016/j.semarthrit.2016.11.004

Objectives
To evaluate the association between smoking and clinical parameters and structural damage in axial spondyloarthritis (axSpA).

Methods
We systematically searched MEDLINE, EMBASE and Cochrane Library up to November 2015. We selected articles that analysed the smoking impact on disease activity, functional status, structural damage, physical mobility and life quality. Independent extraction of articles by 2 authors using predefined data fields was performed. Studies quality was graded according to the Oxford Level of Evidence scale.

Results
A total of 17 articles were selected for inclusion: 2 case-control, 11 cross sectional and 4 prospective cohort studies, which analysed 4,694 patients. Weak evidence suggested a smoking effect on pain, overall assessment of health, disease activity, physical mobility and life quality in ankylosing spondylitis (AS). Moderate-good evidence revealed higher HAQ-AS among smokers (0.025 units/yr, 95%CI: 0.0071–0.0429, p=0.007). Every additional unit of ASDAS resulted in an increase of 1.9 vs. 0.4 mSASSS units/2 yr in AS smokers vs. non-smokers. Good evidence revealed that cigarette smoking and smoking intensity was associated with spinal radiographic progression in axSpA [mSASSS ≥2 units/2 yr: OR=2.75, 95%CI: 1.25–6.05, p=0.012; mSASSS progression in heavy smokers (> 10 cigarettes/day): OR=3.57, 95%IC: 1.33–9.60, p=0.012].

Conclusions
Published data indicate that smoking has a dose-dependent impact on structural damage progression in axSpA. There is worse HAQ among AS smokers compared to non-smokers. Respect to pain, overall assessment of health, disease activity, physical mobility and life quality, although the evidence level is poor, all evidence points in the same direction: smoking AS patients are worse than non-smoking.
LBP

Facet problems

Sonoanatomic indices of lumbar facet joints in patients with facetogenic back pain in comparison to healthy subjects

Journal of Clinical Anesthesia, 12/05/2016

Rahimzadeh P, et al.

Highlights

- There are anatomical changes in patients with FJD.
- Local inflammation increases distance of these joints from the skin.
- Interfacet distance decreases on either side in patients with FJD.
- Ultrasonography provides significant information in facet disease.

Background Nowadays, ultrasound is increasingly used with a great accuracy in performing nerve blocks for facet joint disease.

Objectives To measure sonoanatomic characteristics for the facet joints of lumbar vertebras in patients with facetogenic pain and healthy volunteers.

Study design Cross-sectional, observational study.

Setting University-affiliated Specialty Clinic for Pain Management.

Patients Twenty patients with facet joint disease (FJD) and 40 healthy volunteers (HVGs) were matched for age and sex, height, and weight. Patients with FJD were referred with complaints of pain in the left lumbar facet joints that twice responded favorably to ultrasound guided medial branch blocks.

Intervention Medial branch blocks.

Measurement The interfacet joint distance (IFJD) between the third, the fourth, and the fifth lumbar vertebras and their depth from the level of skin (DFS) were measured bilaterally, using a high-resolution ultrasound in both groups.

Results

Thirty-one men and 29 women with average age of 41.5 ± 9.5 years were enrolled. The IFJD for L3-L4 was 31.5 ± 4.0 mm on the left side and 31.8 ± 4.0 mm on the right side. The IFJD for L4-L5 was 31.3 ± 4.4 mm on the left side and 31.5 ± 4.0 mm on the right side. The IFJD was uniformly 2.2 mm shorter in the FJD group than those in the HVG group (P = .021). The measurements of DFS increased in lower vertebras (L3 < L4 < L5), bilaterally. With an exception of the left facet joints of L4 (P = .016), DFS measurements were similar in FJD and HVG groups.

Limitations

The diagnosis of facet joint disease was merely clinical and the total number of the patients was relatively small.

Conclusion

Interfacet distances of the lumbar vertebras are smaller in patients suffering from degenerative FJD compared with HVGs. Degenerative changes of intervertebral discs and partial reduction of space between 2 adjacent vertebras may contribute to this observation.
7. PELVIC ORGANS/WOMAN’S HEALTH

Vit. D and follicle development

**Effect of vitamin D supplementation on polycystic ovary syndrome: A systematic review and meta-analysis of randomized controlled trials**

Complementary Therapies in Clinical Practice, 11/28/2016

Fang F, et al.

This study was conducted to assess the impact of vitamin D supplementation in patients with PCOS. The analysis of the available data suggests that vitamin D supplementation may be beneficial for follicular development and menstrual cycle regulation in patients with PCOS.

**Methods**

- In this study, the researchers performed a literature search in database and identified all of the RCTs published before December 2015 that compared the impact of vitamin D supplementation with placebo or metformin in PCOS patients.
- 9 out of 463 identified studies were incorporated, including 502 women presenting with PCOS.

**Results**

- According to the findings obtained, vitamin D supplementation had significant impact on the improvement of follicular development with a higher number of dominant follicles (OR, 2.34; 95% CI, 1.39 to 3.92).
- The findings demonstrated that differences in regular menstrual cycles were also seen when metformin plus vitamin D was compared with metformin alone (OR, 1.85; 95% CI, 1.01 to 3.39).
Delivery techniques


Methods of pushing during vaginal delivery and pelvic floor and perineal outcomes: a review.

de Tayrac R¹, Letouzey V.

PURPOSE OF REVIEW:
Over the past 20 years, several randomized studies have compared Valsalva and spontaneous pushing techniques during vaginal delivery. This review summarizes current medical knowledge concerning their maternal and fetal consequences, focusing on pelvic and perineal outcomes.

RECENT FINDINGS:
We selected nine randomized controlled trials comparing Valsalva and spontaneous pushing, and a secondary analysis of a randomized controlled trial comparing different methods of perineal protection. Two trials showed that spontaneous pushing reduces the risk of perineal tears, but no firm conclusions can be drawn given the heterogeneity and inconsistent results of these studies. Conflicting results have been reported regarding the duration of the second stage of labor. Pushing technique does not seem to affect episiotomy, instrumental delivery or cesarean rates. Maternal satisfaction seems to be better after spontaneous pushing. Spontaneous pushing appears to have no adverse effects on neonatal well being, and one study showed a significant improvement in prenatal fetal parameters during the expulsive phase.

SUMMARY:
Valsalva and spontaneous pushing techniques currently appear comparable in terms of duration, pelvic floor, perineal, and neonatal outcomes. In the absence of strong evidence in favor of either technique, the decision should be guided by patient preference and the clinical situation. Additional, well-designed randomized controlled trials are required.
Breastfeeding and diabetes


**Breastfeeding Initiation Associated With Reduced Incidence of Diabetes in Mothers and Offspring.**


**OBJECTIVE:**
To examine associations between breastfeeding initiation and subsequent diabetes among First Nations (indigenous people in Canada who are not Métis or Inuit) and non-First Nations mothers and their offspring with and without gestational diabetes mellitus (GDM).

**METHODS:**
This retrospective database study included 334,553 deliveries (1987-2011) in Manitoba with up to 24 years of follow-up for diabetes using population-based databases. Information of breastfeeding initiation before hospital discharge was obtained from hospital abstracts recorded by nurses in postpartum wards. Cox proportional hazard models were applied to examine the association between breastfeeding initiation and risk of diabetes in mothers and their offspring.

**RESULTS:**
Breastfeeding initiation was recorded in 83% of non-First Nations mothers and 56% of First Nations mothers (P<.001). Breastfeeding initiation was associated with a reduced risk of incident (later developed) diabetes in non-First Nations mothers without GDM (hazard ratio [HR] 0.73 [or -27% of risk], 95% confidence interval [CI] 0.68-0.79), non-First Nations mothers with GDM (HR 0.78 or -22% of risk, CI 0.69-0.89), First Nations mothers without GDM (HR 0.89 or -11% of risk, CI 0.81-0.98), and First Nations mothers with GDM (HR 0.82 or -18% of risk, CI 0.73-0.92) with 24 years of follow-up or less. With 24 years of follow-up or less, breastfeeding initiation was associated with a 17% lower risk of youth-onset type 2 diabetes in offspring (HR 0.83, CI 0.69-0.99, P=.038). The association between breastfeeding initiation and subsequent diabetes in mothers and offspring was independent of family income, rural residence, First Nations status, GDM, parity, gestational hypertension, and age of the mother.

**CONCLUSION:**
Breastfeeding initiation is associated with a reduced risk of diabetes among women and their offspring in Manitoba. The results suggest that breastfeeding might be a potentially modifiable factor to reduce the risk of diabetes in both First Nations and non-First Nations women and children.
8. VISCERA

Transit times


**Mega-Cecum: An Unrecognized Cause of Symptoms in Some Female Patients with Uro-Gynecological Symptoms and Severe Slow Transit Constipation.**

Chey WY, Chang V, Hoellrich CM, Lee KY, Lubkin M, Corcoran D, Chang TM, Chey WD.

**BACKGROUND:**
A subset of female patients with severe constipation report overlapping uro-gynecological symptoms which have been attributed to visceral hypersensitivity.

**AIMS:**
To study colon morphology and motor function in female patients with medically refractory chronic constipation with or without uro-gynecological symptoms and to assess clinical outcomes following laparoscopic ileo-proctostomy.

**METHODS:**
Colon anatomy and cecal emptying time were assessed with plain films and fluoroscopy following a standardized test meal mixed with barium. Transit time was determined with radiopaque markers. IBS-QOL and urinary incontinence questionnaires were employed to assess post-colectomy clinical response.

**RESULTS:**
In 21 consecutive patients, mean colon transit time (h) was 211.1 ± 11.3, which was significantly greater than 58.9 ± 5.1 of 10 normal subjects (P < 0.001). Mega-cecum was found in 15 (Group 1) with mean cecal volume of 587 ± 27.9 cm³, significantly greater (P < 0.001) than 169.5 ± 10.4 cm³ of six without mega-cecum (Group 2). Mean cecal emptying time (days) of barium-mixed feces in Group 1, 4.0 ± 0.6 was significantly greater than 1.33 ± 0.21 in Group 2 (P < 0.001). Eighteen patients (Groups 1 and 2) who had laparoscopic ileo-proctostomy experienced significantly improved quality of life (P < 0.001). In particular, Group 1 patients benefited significantly from improved uro-gynecological symptoms.

**CONCLUSIONS:**
Hitherto an unrecognized mega-cecum with markedly impaired emptying function was found in patients with severe slow transit constipation and uro-gynecological symptoms. Subtotal colectomy relieved constipation and improved significantly uro-gynecological symptoms, suggesting strongly that mega-cecum is causally related to these symptoms.
IBS Fatigue


The contribution of clinical and psychosocial factors to fatigue in 182 patients with inflammatory bowel disease: a cross-sectional study.

Artom M¹, Czuber-Dochan W¹, Sturt J¹, Murrells T¹, Norton C¹,².

BACKGROUND:
Fatigue is a frequently reported and predominant symptom experienced by patients with inflammatory bowel disease (IBD) and its impact has been associated with poorer quality of life (QoL). The complex interplay between disease-related variables and potentially modifiable psychosocial factors in IBD-fatigue has yet to be unravelled.

AIM:
To evaluate the contribution of clinical, sociodemographic and psychosocial factors to the severity and impact of IBD-fatigue and QoL.

METHOD:
In a cross-sectional study, 182 patients with IBD were recruited from three tertiary referral hospitals' out-patient clinics in London. Fatigue was assessed utilising the Inflammatory Bowel Disease-Fatigue Scale (IBD-F), the Multidimensional Fatigue Inventory (MFI); and QoL by the Inflammatory Bowel Disease Questionnaire (IBDQ). Patients completed self-report questionnaires evaluating emotional, cognitive and behavioural factors potentially correlated with fatigue. Sociodemographic data were collected. Disease-related and laboratory data were retrieved from patients' hospital electronic medical records.

RESULT:
In hierarchical regression models, disease activity was the only clinical factor consistently associated with severity and impact of fatigue and QoL (P = 0.01). More negative fatigue perceptions were significantly associated with greater IBD-F1 scores (P = 0.01). When controlling for clinical factors (disease activity and anti-TNF therapy), negative perceptions of fatigue, and all-or-nothing and avoidance behaviours explained an additional 41% of the variance in fatigue impact (IBD-F2).

CONCLUSIONS:
Apart from disease activity, emotional and behavioural factors and patients' negative fatigue perceptions may be key factors to be addressed. Further exploration of these factors in longitudinal and intervention studies may help to develop effective models of fatigue management.
12 B. CERVICAL SURGERIES

Multiple level disc replacements


Jiang L\(^1\), Tan M, Yang F, Yi P, Tang X, Hao Q.

STUDY DESIGN:
This is a systematic review and meta-analysis.

OBJECTIVE:
The aim of this study was to evaluate the efficacy and safety of multiple-level cervical disk replacement (CDR) over single-level CDR for the treatment of cervical spondylosis.

SUMMARY OF BACKGROUND DATA:
Some authors advocate for the multiple-level CDR instead of anterior decompression and fusion in cervical multiple-level spondylosis. However, whether the efficacy and safety of multi-level CDR are as favorable as that of single-level CDR remains controversial.

METHODS:
MEDLINE, EMBASE, and Cochrane library databases were searched up to November 2015 for controlled studies that compared the clinical outcomes of single-level and multiple-level CDR for the treatment of cervical spondylosis. The following outcomes were extracted and analyzed: prevalence of heterotopic ossification and reoperation rate, preoperative and postoperative Neck Disability Index scores, preoperative and postoperative Visual Analog Scale scores, and success rate using the Odom grading system.

RESULTS:
Ten studies involving 1402 patients were included: including 3 randomized controlled trials, 5 prospective studies, and 3 retrospective studies. No significant differences between single-level and multiple-level groups were found in terms of the prevalence of heterotopic ossification and reoperation rate, Neck Disability Index score, Visual Analog Scale score, and success rate using the Odom grading system.

CONCLUSIONS:
On the basis of this meta-analysis, clinical outcomes of multiple-level CDR are similar to those of single-level CDR for cervical spondylosis, which suggests the multiple-level CDR is as effective and safe as the single-level CDR. Nonetheless, more well-designed studies are needed for further evaluation.
13. CRANIUM/TMJ

Airways and orthodontics


Effect of orthodontic treatment on the upper airway volume in adults.
Pliska BT\(^1\), Tam IT\(^2\), Lowe AA\(^3\), Madson AM\(^4\), Almeida FR\(^5\).

INTRODUCTION:
The aim of this study was to examine the effects of orthodontic treatment with and without extractions on the anatomic characteristics of the upper airway in adults.

METHODS:
For this retrospective study, the pretreatment and posttreatment cone-beam computed tomography scans of 74 adult patients meeting defined eligibility criteria were analyzed. Imaging software was used to segment and measure upper airway regions including the nasopharynx, the retropalatal, and retroglossal areas of the oropharynx, as well as the total airway. The Wilcoxon signed rank test was used to compare volumetric and minimal cross-sectional area changes from pretreatment to posttreatment.

RESULTS:
The reliability values were high for all measurements, with intraclass correlation coefficients of 0.82 or greater. The volumetric treatment changes for the extraction and nonextraction groups were as follows: total airway, \(1039.6 \pm 3674.3 \text{ mm}^3\) vs \(1719.2 \pm 4979.2 \text{ mm}^3\); nasopharynx, \(136.1 \pm 1379.3 \text{ mm}^3\) vs \(-36.5 \pm 1139.8 \text{ mm}^3\); retropalatal, \(412.7 \pm 3042.5 \text{ mm}^3\) vs \(399.3 \pm 3294.6 \text{ mm}^3\); and retroglossal, \(412.5 \pm 1503.2 \text{ mm}^3\) vs \(1109.3 \pm 2328.6 \text{ mm}^3\). The treatment changes in volume or minimal cross-sectional area for all airway regions examined were not significantly (P >0.05) different between the extraction and nonextraction groups.

CONCLUSIONS:
Orthodontic treatment in adults does not cause clinically significant changes to the volume or the minimally constricted area of the upper airway. These results suggest that dental extractions in conjunction with orthodontic treatment have a negligible effect on the upper airway in adults.
Erectile dysfunction and oral health


Chronic periodontitis and the risk of erectile dysfunction: a systematic review and meta-analysis.

Liu LH1, Li EM1, Zhong SL2, Li YQ3, Yang ZY4, Kang R1, Zhao SK1, Li FT1, Wan SP1, Zhao ZG1.

The objective of this study is to evaluate the association between chronic periodontitis (CP) and the risk of erectile dysfunction (ED).

Electronic search using PubMed, Embase and the Cochrane Library was carried out for observational studies, longitudinal, cohort, case-control and epidemiological studies on humans, published up to December 2015. Manual searches were also performed. Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were used to estimate the association between CP and the risk of ED. Methodological quality assessment was carried out using the Newcastle-Ottawa Quality Assessment Scale. Four case-control studies and one cross-sectional study involving 213,006 participants were included. Based on the random-effects model, analyses of all studies showed that CP was associated with an increased risk of ED (OR=2.28, 95% CI: 1.50-3.48). There was heterogeneity among the studies (P<0.001, I²=97.8%). Estimates of total effects were generally consistent with the sensitivity and subgroup analyses.

In conclusion, our meta-analysis suggested that there was a significant association between CP and the risk of ED. Further epidemiological studies are needed to better estimate the key risk factors for periodontitis and their interaction effects.

International Journal of Impotence Research advance online publication, 10 November 2016; doi:10.1038/ijir.2016.43.
Osseous osteoarthritic-like changes and joint mobility of the temporomandibular joints and upper cervical spine - Is there a relation?

Objectives
To compare 1) temporomandibular joint (TMJ) mobility between subjects a) with and without reduced upper cervical spine (UCS) mobility and b) with and without TMJ osseous osteoarthritic-like changes; and 2) UCS osseous changes between subjects a) with and without TMJ osseous osteoarthritic-like changes and b) with and without reduced UCS mobility.

Study design
39 subjects without pain from TMJ and UCS including 15 women (26-72 years, mean 56.0) and 24 men (27-71 years, mean 49.8) with obstructive sleep apnea (OSA) comprised the patient population. The range of motion (ROM) of the mandible and UCS was assessed clinically. Osseous changes of the TMJ and UCS were assessed by cone beam computed tomography. Differences were tested and adjusted for age and gender by multiple linear and logistic regression analyses.

Results
The mandibular ROM was within normal range (45-64 mm) but the UCS ROM was reduced in 15 subjects. Osseous TMJ and UCS changes were both found in 38.5% of the subjects. Osseous UCS changes were more frequent in subjects with than without TMJ changes (P=0.0003; Odds Ratio (OR) 21.9). No other significant results were found.

Conclusions
The present findings in OSA patients of co-morbid osseous changes support a possible biomechanical relationship between the TMJs and UCS.
Assessment of the Trabecular Structure of Mandibular Condyles in Patients with Temporomandibular Disorders Using Fractal Analysis

Belde Arsan Taha Emre Köse Erhan Çene İlknur Özcan

DOI: http://dx.doi.org/10.1016/j.oooo.2016.11.005

Objectives
The aim of this study was to evaluate changes in the trabecular structure of the mandibular condyle in patients with temporomandibular disorders (TMD) using fractal analysis (FA).

Study Design
A total of 100 patients aged between 18-73 years were clinically assessed with the Diagnostic Criteria for Temporomandibular Disorders. The control group was age- and sex matched with the patient group. Panoramic radiographs were obtained using a Kodak 8000 digital device with 73 kVp and 5 mA fixed parameters. The degree of degeneration in the mandibular condyles was calculated. Regions of interest (84x84 pixels) were selected within the cortical boundary of the mandibular condyle and the fractal dimension (FD) was calculated using ImageJ version 1.48.

Results
Radiographic degenerative changes were present more frequently and were more severe in the patient group (p<0.001). The mean value of FD was 1.22±0.06 in the patient group and 1.25±0.06 in the control group (p= 0.001). In the left TMJs of the patient group, a significant decrease in FD was observed (p= 0.001), whereas an insignificant decrease in FD was observed in the right TMJs (p= 0.073) as degenerative changes increased.

Conclusions
Lower values of FD were associated with more severe degenerative changes in the patient group. The trabecular structure of condyles in patients with TMD exhibited decreased complexity when erosive and sclerotic changes were evident. As a result, FA enhanced the use of panoramic radiography in the detection of degenerative changes in patients with TMD.
TMJ and bruxism


**Prosthodontic planning in patients with temporomandibular disorders and/or bruxism: A systematic review.**
Manfredini D1, Poggio CE2.

**STATEMENT OF PROBLEM:**
The presence of temporomandibular disorders (TMDs) and/or bruxism signs and symptoms may present multifaceted concerns for the prosthodontist.

**PURPOSE:**
The purpose of this systematic review was to evaluate the relationship between prosthetic rehabilitation and TMDs and bruxism.

**MATERIAL AND METHODS:**
Three research questions were identified based on different clinical scenarios. Should prosthodontics be used to treat TMD and/or bruxism? Can prosthodontics cause TMDs and/or bruxism? How can prosthodontics be performed (for prosthetic reasons) in patients with TMDs and/or bruxism? A systematic search in the PubMed database was performed to identify all randomized clinical trials (RCTs) comparing the effectiveness of prosthodontics with that of other treatments in the management of TMDs and/or bruxism (question 1); clinical trials reporting the onset of TMDs and/or bruxism after the execution of prosthetic treatments in healthy individuals (question 2); and RCTs comparing the effectiveness of different prosthodontics strategies in the management of the prosthetic needs in patients with TMDs and/or bruxism (question 3).

**RESULTS:**
No clinical trials of the reviewed topics were found, and a comprehensive review relying on the best available evidence was provided. Bruxism is not linearly related to TMDs, and both of these conditions are multifaceted. Based on the diminished causal role of dental occlusion, prosthetic rehabilitation cannot be recommended as a treatment for the 2 conditions. In theory, they may increase the demand for adaptation beyond the stomatognathic system's tolerability. No evidence-based guidelines were available for the best strategy for managing prosthetic needs in patients with TMDs and/or bruxism.

**CONCLUSIONS:**
This systematic review of publications revealed an absence of RCTs on the various topics concerning the relationship between TMD and bruxism and prosthodontics. Based on the best available evidence, prosthetic changes in dental occlusion are not yet acceptable as strategies for solving TMD symptoms or helping an individual stop bruxism. Clinicians should take care when performing irreversible occlusal changes in healthy individuals and in patients with TMD and/or bruxism.
Botox


Clinical outcomes of Botox injections for chronic temporomandibular disorders: do we understand how Botox works on muscle, pain, and the brain?
Connelly ST1, Myung J2, Gupta R2, Tartaglia GM3, Gizdulich A3, Yang J4, Silva R2.

The main objective of this retrospective review was to analyze the clinical outcomes following the use of botulinum toxin (onabotulinumtoxinA, Botox) injections to relieve the symptoms of chronic temporomandibular disorders (TMD).

Seventy-one patients with a diagnosis of TMD (according to the RDC/TMD international consortium) associated with or without bruxism and refractory to conventional treatment (e.g. oral appliances, physiotherapy, etc.) received Botox injections into the temporalis and masseter muscles. Subjective responses to Botox were categorized as 'beneficial' or 'not beneficial', as patient-reported outcomes based on the subjective reduction in pain and/or improvement in function. Fifty-five of the 71 subjects (77%) reported beneficial effects with Botox. Subjects with a concomitant bruxism diagnosis reported significant improvement over subjects without bruxism (87% vs. 67%; P=0.042). Subjects with stress-related psychiatric comorbidities and bruxism had a significantly higher benefit than those with stress-related psychiatric comorbidities alone (P=0.027).

Patients reported less improvement if the time between the initial Botox injection and follow-up was less than an average of 5 weeks, compared to an average follow-up of 5-10 weeks (P=0.009). The subgroup TMD diagnosis and time interval post-injection are important predictors of patient-reported beneficial outcomes.
Sugar drinks and tooth loss


**Permanent tooth loss and sugar-sweetened beverage intake in U.S. young adults.**
Kim S1, Park S2, Lin M3.

**OBJECTIVE:**
In young adults, sugar-sweetened beverage (SSB) intake is associated with dental caries, which in turn is a major contributor to tooth loss. The independent role of SSB intake on tooth loss, however, has not been well-described. This cross-sectional study examined associations between tooth loss and SSB intake among U.S. young adults.

**METHODS:**
The outcome was number of permanent teeth lost because of dental caries or periodontal disease (0, 1-5, ≥6 teeth). Data from the 2012 Behavioral Risk Factor Surveillance System were used. The 22,526 adults aged 18-39 years completed the Sugar Drink Module. The exposure variable was daily frequency of SSB intake. We used multinomial logistic regression to examine the adjusted associations between tooth loss and daily SSB consumption (0, >0 to <1, 1-2, >2 times/day).

**RESULTS:**
Approximately, 26% of young adults reported losing at least one permanent tooth. Tooth loss was positively associated with SSB intake frequency; the odds of losing 1-5 teeth were higher among adults drinking SSBs >0 to <1 times/day (OR = 1.44, 95%CI = 1.16-1.79), 1-2 times/day (OR = 1.58, 95%CI = 1.25-1.99), and >2 times/day (OR = 1.97, 95%CI = 1.51-2.58) than non-SSB consumers. The odds of losing ≥6 teeth were higher among adults drinking SSBs 1-2 times/day (OR = 2.20, 95%CI = 1.15-4.22) and >2 times/day (OR = 2.81, 95%CI = 1.37-5.76) than non-SSB consumers.

**CONCLUSIONS:**
Frequency of SSB consumption was positively associated with tooth loss among young adults even when the average SSB intake was less than one time per day. This study suggests that efforts to reduce SSB intake among young adults may help to decrease the risk of tooth loss.
Fascial asymmetry


**Defining the location of the dental midline is critical for oral esthetics in camouflage orthodontic treatment of facial asymmetry.**

Kai R¹, Umeki D², Sekiya T³, Nakamura Y⁴.

When considering camouflage orthodontic treatment of a malocclusion associated with significant facial asymmetry, it is important to define the location of the dental midline.

The patient, a 19-year-old Japanese woman, had an anterior open bite and a dental midline discrepancy associated with facial asymmetry. A nonsurgical treatment plan was considered. The main treatment objective was to correct the anterior open bite and the dental midlines in both arches. The dental midline discrepancy was eliminated, and proper overjet and overbite were achieved. Although the facial asymmetry remained, oral esthetics dramatically improved and a favorable occlusion was obtained.

The results suggest that appropriately defining the location of the dental midline is critical for successful camouflage treatment of facial asymmetry.
14. HEADACHES

Migraine frequency

Migraine affects 1 in 10 people worldwide featuring recent rise: A systematic review and meta-analysis of community-based studies involving 6 million participants

Journal of the Neurological Sciences, 12/08/2016

Woldeamanuel YW, et al.

In this meta–analysis, the physicians aim to study the weighted average global prevalence of migraine at the community level. As per this systematic review, migraine influences 1 in 10 people worldwide featuring recent rise. They found higher prevalence among females, students, and urban residents.

Methods

- The physicians conducted a systematic review using advanced search strategies employing PubMed/MEDLINE, Scopus, and Web of Science for community-based and non-clinical studies by combining the terms “migraine”, “community-based”, and names of every country worldwide spanning all previous years from January 1, 1920 until August 31, 2015.
- Methods were in accordance with PRISMA and MOOSE guidelines.
- They performed a meta-analysis with subgroup analysis to identify pooled migraine prevalence and examine cohort heterogeneity.

Results

- The physicians included 302 community-based studies involving 6,216,995 participants (median age 35 years, male-to-female ratio of 0.91).
- As per the outcomes, global migraine prevalence was 11.6% (95% CI 10.7–12.6%; random effects); 10.4% in Africa, 10.1% in Asia, 11.4% in Europe, 9.7% in North America, 16.4% in Central and South America.
- The prevalence was 13.8% among females, 6.9% among males, 11.2% among urban residents, 8.4% among rural residents, and 12.4% among school/college students when the pooled cohort was stratified.
- The outcome demonstrated a pattern of rising global migraine prevalence.
ABSTRACTS

Migraines and stroke


Assessment of Migraine History in Patients with a Transient Ischemic Attack or Stroke; Validation of a Migraine Screener for Stroke.

van der Willik D1, Pelzer N, Algra A, Terwindt GM, Wermer MJ.

BACKGROUND:
To investigate the connection between migraine and stroke, a reliable screening tool to gather information about a person's migraine history is crucial. We studied the test-characteristics of a 5-question Migraine Screener for Stroke (MISS).

METHODS:
We included a random sample of patients with a transient ischemic attack or stroke who answered the MISS questionnaire when they were admitted to our hospital. After discharge, a semi-structured telephone interview was conducted to validate the migraine diagnosis with the International Classification of Headache Disorders, second-edition criteria as gold standard.

RESULTS:
Forty-nine (22.2%) of the 221 included patients were diagnosed with life-time migraine (38.5% women, 7.7% men). The sensitivity of all questions combined was 0.47 (95% CI 0.31-0.62), the specificity was 0.97 (95% CI 0.93-0.99), the positive predictive value (PPV) was 0.80 (95% CI 0.59-0.93) and the negative predictive value (NPV) was 0.87 (95% CI 0.82-0.92). One question related to the presence of headache accompanied by hypersensitivity to lights and sounds had a better sensitivity (0.96, 95% CI 0.85-1.00) and NPV (0.99, 95% CI 0.95-1.00) than all questions put together. For assessing migraine with aura, the question about visual disturbances had a good NPV (0.99, 95% CI 0.96-1.00), but a low PPV (0.38, 95% CI 0.24-0.53).

CONCLUSIONS:
The MISS questionnaire can be used by researchers to rule out migraine history in stroke patients. To prevent misclassification, especially for the aura symptoms, patients with a positive screener should be interviewed more extensively to confirm the migraine diagnosis.
Psychosocial factors associated with migraine and tension-type headache in medical students

**Background** In our previous study of workers, blood donors and medical students, students stood out with a higher 1-year prevalence of migraine (28%) and tension-type headache (TTH) (74%). General factors associated with headache were common for all groups except low physical activity. The hypothesis of this study was therefore that a number of psychosocial factors relating to the personal sphere would better explain the high prevalence of migraine and TTH in students.

**Methods** The study population consisted of 1042 students (719 females, 323 males, mean age 20.6, range 17–40). Headache diagnoses and associated factors were identified by direct professional semi-structured interview. We also interviewed about the following psychosocial factors: dissatisfaction with study, dissatisfaction with family life, dissatisfaction for personal reasons, bad financial situation, overwork, stress, not enough sleep, insomnia, depressed mood, anxiety, irritability, tendency towards conflicts and not being married. We report psychosocial factors associated with headache according to diagnosis and sex using univariate and multivariate logistic regression analyses.

**Results** Several factors were significantly associated with migraine and TTH in the univariate analysis. In the multivariate analysis, two psychosocial factors were statistically significantly associated with migraine in all students: irritability (OR 2.2, 95% CI 1.4–3.6) and overwork (OR 2.2, 95% CI 1.4–3.5). Insomnia (2.7, 95% CI 1.1–6.9) and depressed mood (OR 2.1, 95% CI 1.1–4.2) were associated with migraine only in females. Two psychosocial factors were associated with TTH: dissatisfaction with study in males (OR 2.0, 95% CI 1.0–3.8) and depressed mood in females (OR 1.8, 95% CI 1.0–3.5).

**Conclusion** Psychosocial factors from the personal sphere showed significant association with migraine and TTH in students. Such factors should therefore be major targets for preventive efforts to reduce the prevalence of primary headache disorders in students.
Migraines in women who live together


**Women Living Together Have a Higher Frequency of Menstrual Migraine.**

Ferreira KS¹, Guilherme G², Faria VR², Borges LM², Uchiyama AA².

**BACKGROUND:**
Menstrual migraine is a highly prevalent disorder among adult women, resulting in disability and loss of quality of life. Some studies have reported menstrual cycle synchrony among women living together. No study has reported whether there may also be a higher prevalence of menstrual migraine among these women. Thus, they reported here the prevalence of menstrual migraine in a group of women living together compared with a control group of women living alone, and discussed the possible factors involved.

**METHODS:**
The study was conducted on female university students aged 18-30 years with a diagnosis of migraine according to the criteria of the International Classification of Headache Disorders III, beta appendix criteria. The subjects were divided into a group of women who lived together with two or more other students and a control group of age-matched students who lived alone, interviewed with a specific questionnaire and assessed for 3 months by means of a paper pain diary. The data evaluated included frequency of headache, presence of menstrual migraine, intensity of headache, medications used including contraceptives, and triggering factors such as diet, sleep deprivation, and stress. The menstrual data and data related to migraine were also investigated in the roommates.

**RESULTS:**
A higher occurrence of menstrual migraine among women living together (9, 50%) compared with women living alone (3, 16.7%) (P = .03) was detected. After binary logistic regression analysis, this finding was not related to the main influencing factors detected, that is, use of a contraceptive, test stress, or sleep deprivation (P = .03, adjusted odds ratio: 7.87; 1.23-50.36). These women also showed menstrual cycle synchrony with their roommates (8, 44.4%) and the presence of headache crises during the menstruation of their colleagues (11, 61.1%).

**CONCLUSION:**
The present study detected a higher occurrence of menstrual migraine among women who lived together. Since there was no previous description of this topic in the literature, it was believed that the present study could represent a step toward more elaborate investigations of this complex topic.
Opioid use


Risk of medication overuse headache across classes of treatments for acute migraine.
Thorlund K1,2, Sun-Edelstein C3, Druyts E4,5, Kanters S4,6, Ebrahim S7, Bhambri R8, Ramos E8, Mills EJ7,4, Lanteri-Minet M9,10, Tepper S11.

BACKGROUND:
The most commonly prescribed medications used to treat migraine acutely are single analgesics, ergots, opioids, and triptans. Due to varying mechanisms of action across drug classes, there is reason to believe that some classes may be less likely than others to elicit Medication Overuse Headache (MOH) than others. We therefore aimed to determine whether certain classes of acute migraine drugs are more likely to elicit MOH than others.

METHODS:
A comprehensive systematic literature was conducted to identify studies of varying designs that reported on MOH within the considered treatment classes. Only studies that reported MOH according to the International Classification of Headache Disorders (ICHD) were considered. Since no causal comparative design studies were identified; data from prevalence studies and surveys were retrieved. Prevalence-based relative risks between treatment classes were calculated by integrating both medication overuse and medication use from published studies. For each pairwise comparison, pooled relative risks were calculated as the inverse variance weighted average.

RESULTS:
A total of 29 studies informed the relative risk between treatment classes, all of which reported country-specific data. Five studies reported country-specific medication use data. For triptans versus analgesics the study relative risks generally favored triptans. The pooled relative risk was 0.65 (i.e., relative risk reduction of 35%). For ergots versus analgesics, a similar trend was observed in favor of ergots with a relative risk of 0.41. For triptans versus ergots, the direction of effect was mixed, and the pooled relative risk was 1.07. Both triptans and ergots appeared favorable when compared to opioids, with pooled relative risks of 0.35 and 0.76, respectively. However, the evidence was limited for these comparisons. Analgesics and opioids also appeared to yield similar risk of MOH (pooled relative risk 1.09).

CONCLUSION:
Our study suggests that in patients receiving acute migraine treatment, analgesics and opioids are associated with a higher risk of developing MOH compared with other treatments. These findings provide incentive for better monitoring of use of analgesics and opioids for treating acute migraine, and suggest possible clinical preference for use of so-called "migraine-specific" treatments, that is, triptans and ergots
16. CONCUSSIONS

Young NFL players concussions

Evidence of Brain Injury Found in Young NFL Players

*PET scan of a healthy human brain.*

In a small study of young or recently retired NFL players, researchers at Johns Hopkins report finding evidence of brain injury and repair that is visible on imaging from the players compared to a control group of men without a history of concussion.

In a report on the study that used positron emission tomography (PET) and MRI, published in *JAMA Neurology* on Nov. 28, the researchers highlighted the value of PET imaging to monitor a marker of injury and repair in the brains of NFL players and athletes in other contact sports. The new research builds on a rising tide of anecdotal evidence and a few scientific studies suggesting that people with repeated concussive head injuries incurred while playing football, hockey or boxing are at higher-than-normal risk of developing the neurodegenerative disease called chronic traumatic encephalopathy (CTE). CTE is associated with memory deficits, confusion, poor decision-making and later onset of dementia.

However, because CTE is often only diagnosed at autopsy, and because similar symptoms may occur in people without repeated head injuries, researchers, including those at Johns Hopkins Medicine, have been developing methods to better visualize tissue damage in the living brain to demonstrate better cause and effect.

“The exciting part of our new findings is that we now believe we have a useful tool to monitor the brains of NFL players and athletes in other contact sports,” says Jennifer Coughlin, M.D., assistant professor of psychiatry and behavioral sciences at Johns Hopkins. “We can measure TSPO, a PET biomarker of brain injury, in these younger players, and we can now begin to follow it over time to see if the brain is repairing itself or not.”

In early 2015, the Johns Hopkins research team published PET imaging results showing higher levels of this same biomarker in the brains of nine elderly former NFL players compared to control participants. However, since they initially studied elderly players who were many years from play, the researchers were unable to tell if the findings were also linked to aging and vascular disease, independent of past NFL play.

For the new study, the researchers collected PET imaging data from 11 men without a history of concussion and compared the scans to those of 12 young NFL players, all of whom were still active or had retired within the past 12 years. All players had a self-reported history of at least one concussion. These players were an average age of 31 years old. About 80 percent were Caucasian and 20 percent were African-American. The control participants were matched to the players by body mass index, age and education level.

The PET imaging was acquired using a radioactive chemical that binds to translocator protein 18 kDa (TSPO), which is normally found at low levels in healthy brain tissue. Since TSPO is increased during cellular response to brain injury, high levels of the TSPO signal on each PET scan can indicate where injury and reparative processes occur.

The researchers found higher radiotracer binding to TSPO in players compared to control participants in eight of the 12 brain regions studied. These regions included the hippocampus, a region functionally involved in memory.

Separately, the researchers examined data from MRI scans to look for structural changes in the brains of the study participants. They found no evidence of brain tissue loss in players compared
to control participants in any of the brain regions examined, yet they did find some evidence of white matter changes in the players’ brains.

“We suspect that when the brain moves during a hard hit, it causes a shearing injury of the white matter fibers that travel across the brain,” says Coughlin. Coughlin cautioned that there are some limitations to the imaging technique. For example, the radiotracer used in the PET scans doesn’t work well in people with a specific variation in the gene that codes for TSPO protein, which occurs in about one in 10 people of European descent. Also, the researchers observed that use of creatine supplements — taken by athletes to improve performance — may interfere with the imaging results, necessitating further study of this effect before including participants taking creatine.

“With further research using this technology, we may better understand the relationship between concussion and brain damage,” says Coughlin. “Further understanding may help inform players of associated risk, and will allow us to test preventive and therapeutic interventions that may improve the lives of players.”

According to Centers for Disease Control and Prevention estimates, anywhere from 1.6 to 3.8 million concussions happen each year in the U.S. because of sports or recreational activities. Other researchers contributing to the study include Yuchuan Wang, Il Minn, Nicholas Bienko, Emily Ambinder, Xin Xu, Matthew Peters, John Dougherty, Melin Vranesic, Soo Min Koo, Hye-Hyun Ahn, Merton Lee, Chris Cottrell, Haris Sair, Akira Sawa, Cynthia Munro, Robert Dannals, Constantine Lyketsos, Gwenn Smith, Brian Caffo, Susumu Mori and Martin Pomper of The Johns Hopkins University; Christopher Nowinski of Boston University; Michael Kassiou of the University of Sydney; and Tomas Guilarte of Florida International University.
20 A. ROTATOR CUFF

Acute vs chronic repair


Comparison of outcomes with arthroscopic repair of acute-on-chronic within 6 months and chronic rotator cuff tears.
Jeong JY¹, Song SY¹, Yoo JC², Park KM¹, Lee SM³.

BACKGROUND:
The purpose of this study was to define preoperative and intraoperative findings of acute-on-chronic rotator cuff tears (RCTs). This study also compared the functional and clinical outcomes with acute-on-chronic RCTs and chronic RCTs.

METHODS:
This study was conducted between December 2007 and December 2013. An acute-on-chronic full-thickness RCT was diagnosed with preoperative and intraoperative findings on arthroscopy. The study group consisted of 36 patients with preoperative and intraoperative findings (surgery performed within 6 months of trauma) indicative of an acute-on-chronic RCT. Another 36 patients matched for age, sex, and tear size, who underwent arthroscopic rotator cuff repair after 6 months of onset of symptoms (chronic RCT group), were selected from our institution's database within the same time frame. Postoperative indirect magnetic resonance arthrogram was obtained 6 months after the repair, and rotator cuff integrity was graded according to the guidelines as described by Sugaya. Patients were evaluated using the visual analog scale for pain, American Shoulder and Elbow Surgeons Shoulder Assessment score, and Constant scores. Scores and measurements were obtained preoperatively and at 6, 12, and 24 months after surgery.

RESULTS:
The clinical outcomes and range of motion recovery were better in the acute-on-chronic RCT group. Although statistically not significant, the acute-on-chronic RCT group's repair appeared closer to the complete repair and was associated with a lesser incidence of retear than the chronic RCT group.

CONCLUSION:
Early repair of an acute-on-chronic full-thickness RCT results in a statistically and clinically superior improvement in outcomes compared with repairs of chronic RCTs.
24. ELBOW

Isometrics for lateral epicondylalgia


**Isometric Exercise Above but not Below an Individual's Pain Threshold Influences Pain Perception in People With Lateral Epicondylalgia.**

Coombes BK¹, Wiebusch M, Heales L, Stephenson A, Vicenzino B.

**OBJECTIVE:**
To examine the acute effects of isometric exercise of different intensities on pain perception in individuals with chronic lateral epicondylalgia.

**MATERIALS AND METHODS:**
Participants performed 3 experimental tasks completed in a randomized order on separate days: control (no exercise) and isometric wrist extension (10×15 s) at load 20% below (infrathreshold), and 20% above (suprathreshold) an individual's pain threshold. Self-reported pain intensity (11-point numeric rating scales), pressure pain threshold, and pain-free grip were assessed by a blinded examiner before, immediately after, and 30 minutes after task performance. Relation analysis between pain ratings and clinical variables, including pain and disability and kinesiophobia was performed.

**RESULTS:**
Twenty-four individuals with unilateral lateral epicondylalgia of median 3-month duration participated. Pain intensity during contraction was significantly higher during suprathreshold exercise than infrathreshold exercise (mean difference in numeric rating scale 1.0; 95% confidence interval, 0.4-1.5; P=0.002). Pain intensity during suprathreshold exercise was significantly correlated with pain and disability (R=0.435, P=0.034) and kinesiophobia (R=0.556, P=0.005). Pain intensity was significantly higher immediately after performance of suprathreshold exercise, compared with infrathreshold exercise (P<0.01) and control (P<0.001) conditions, whereas infrathreshold exercise and control conditions were comparable. Thirty minutes later, pain levels remained significantly higher for suprathreshold exercise compared with infrathreshold exercise (P=0.043). Pressure pain threshold and pain-free grip showed no significant effects of time, condition, or timexcondition (P>0.05).

**DISCUSSION:**
Individuals with lateral epicondylalgia demonstrated increased pain intensity after an acute bout of isometric exercise performed at an intensity above, but not below, their individual pain threshold. Further investigation is needed to determine whether measurement of an individual's exercise induced pain threshold may be important in reducing symptom flares associated with exercise.
26. CARPAL TUNNEL SYNDROME

Use of flax seed oil


A Topical Gel From Flax Seed Oil Compared With Hand Splint in Carpal Tunnel Syndrome: A Randomized Clinical Trial.

Setayesh M¹, Sadeghifar AR², Nakhaee N², Kamalinejad M³, Rezaeizadeh H⁴.

This study compared the therapeutic effect of flax seed oil topical gel and hand splint in the treatment of carpal tunnel syndrome.

This study was a randomized clinical trial. Forty-nine patients, 96 hands, with mild to moderate idiopathic carpal tunnel syndrome were divided into 2 groups randomly. One group was treated by topical gel and the other group by hand splint. Intensity of symptoms and function before and after intervention was measured via Boston Carpal Tunnel Questionnaire. After intervention, the ANCOVA showed a significant difference between the symptom and function scores of the 2 groups. In both cases, recovery was higher in the gel group (P < .001).

The topical use of flax seed oil gel is more effective in the improvement of symptoms and function of patients with mild to moderate carpal tunnel syndrome as compared with hand splint, and it can be introduced as an effective treatment.
Experts outline importance of recognizing, treating meniscal root tears

Baylor College of Medicine News, 12/08/2016

Tears of the root of the meniscus have been increasingly recognized in recent years, which is why physicians at Baylor College of Medicine recently published a paper in the journal RadioGraphics that stresses the importance of recognizing and treating these tears.

“Tears at the root of the lateral or medial meniscus can be a cause of knee pain, and while a root tear might be suspected during an exam, an MRI scan is the best diagnostic modality of picking up these injuries,” said Dr. Theodore Shybut, assistant professor of orthopedic surgery at Baylor and a co–author of the paper.

Lateral meniscal root tears often occur with knee instability associated with anterior cruciate ligament (ACL) tears. Shybut’s research has shown that the lateral meniscal root is a secondary stabilizer of the ACL. Medial meniscal root tears can be associated with trauma, but also often occur in the setting of cartilage thinning and degenerative joint disease.

Biomechanical studies have shown a meniscal root tear is similar to not having a functional meniscus at all, which is associated with accelerated development of arthritis.

“The biomechanics research suggests that if you can repair the root and get it to heal, you may help postpone osteoarthritis of the knee on the medial side. On the lateral side, you are usually addressing instability,” said Shybut.

In this new paper, Shybut and colleagues emphasize the importance of recognizing these injuries through MRIs, give tools for how to communicate the injury between radiologists and surgeons and also describe surgical technique and post–operative imaging.

“Raising awareness of these injuries is important so radiologists and surgeons are looking for them,” said Shybut.
Increasing frequency


**Substantial rise in the lifetime risk of primary total knee replacement surgery for osteoarthritis from 2003 to 2013: an international, population-level analysis.**

Ackerman IN¹, Bohensky MA², de Steiger R³, Brand CA⁴, Eskelinen A⁵, Fenstad AM⁶, Furnes O⁷, Garellick G⁸, Graves SE⁹, Haapakoski J¹⁰, Havelin LI¹¹, Mäkelä K¹², Mehnert F¹³, Pedersen AB¹⁴, Robertsson O¹⁵.

**OBJECTIVE:**
To estimate and compare the lifetime risk of total knee replacement surgery (TKR) for osteoarthritis (OA) between countries, and over time.

**METHOD:**
Data on primary TKR procedures performed for OA in 2003 and 2013 were extracted from national arthroplasty registries in Australia, Denmark, Finland, Norway and Sweden. Life tables and population data were also obtained for each country. Lifetime risk of TKR was calculated for 2003 and 2013 using registry, life table and population data.

**RESULTS:**
Marked international variation in lifetime risk of TKR was evident, with females consistently demonstrating the greatest risk. In 2013, Finland had the highest lifetime risk for females (22.8%, 95%CI 22.5-23.1%) and Australia had the highest risk for males (15.4%, 95%CI 15.1-15.6%). Norway had the lowest lifetime risk for females (9.7%, 95%CI 9.5-9.9%) and males (5.8%, 95%CI 5.6-5.9%) in 2013. All countries showed a significant rise in lifetime risk of TKR for both sexes over the 10-year study period, with the largest increases observed in Australia (females: from 13.6% to 21.1%; males: from 9.8% to 15.4%).

**CONCLUSIONS:**
Using population-based data, this study identified significant increases in the lifetime risk of TKR in all five countries from 2003 to 2013. Lifetime risk of TKR was as high as 1 in 5 women in Finland, and 1 in 7 males in Australia. These risk estimates quantify the healthcare resource burden of knee OA at the population level, providing an important resource for public health policy development and healthcare planning.
Measuring recovery


Assessing functional recovery shortly after knee or hip arthroplasty: a comparison of the clinimetric properties of four tools.

Poitras S\(^1\), Wood KS\(^2\), Savard J\(^3\), Dervin GF\(^2\), Beaulé PE\(^2\).

BACKGROUND:
Following hip or knee arthroplasty, it is clinically warranted to get patients functional as quickly as possible. However, valid tools to assess function shortly after knee or hip arthroplasty are lacking. The objective was to compare the clinimetric properties of four instruments to assess function shortly after arthroplasty.

METHODS:
One hundred eight patients undergoing hip or knee arthroplasty were assessed preoperatively, 1 and 2 days postoperatively, and 2 and 6 weeks postoperatively with the Timed Up and Go (TUG), Iowa Level of Assistance Scale (ILAS), Postoperative Quality of Recovery Scale (PQRS), and Readiness for Hospital Discharge Scale (RHDS). Descriptive data, floor and ceiling effects, responsiveness, interpretation and construct validity were determined.

RESULTS:
Only the ILAS and RHDS support subscale demonstrated floor or ceiling effects. A large deterioration from preoperative to postoperative, followed by large improvements after surgery were seen in the TUG and ILAS scores. The RHDS personal status subscale and the PQRS pain and function dimensions demonstrated large improvements after surgery. Changes in the RHDS global scale and personal status subscale, PQRS pain dimension and TUG were significantly related to patient perceived improvement. Minimal important changes were obtained for the RHDS global (1.1/10) and personal status subscale (2.3/10), and the TUG (43.4 s at 6 weeks). For construct validity, the PQRS function dimension and RHDS were moderately related to the TUG or ILAS. The correlation between TUG and ILAS was high from preoperative to postoperative day 2, but substantially decreased at 2 and 6 weeks.

CONCLUSIONS:
The TUG and RHDS personal status subscale demonstrated the best clinimetric properties to assess function in the first 6 weeks after hip or knee arthroplasty.
37. OSTEOARTHRITIS/KNEE

Lack of adherence to care


Barriers for guideline adherence in knee osteoarthritis care: A qualitative study from the patients’ perspective.

Spitaels D1, Vankrunkelsven P1, Desfosses J2, Luyten F3, Verschueren S4, Van Assche D3, Aertgeerts B1, Hermens R1,5.

RATIONALE, AIMS AND OBJECTIVES:
Guidelines for patients with knee osteoarthritis (OA) are suboptimally implemented in clinical care. To improve guideline adherence, patients’ perceived barriers and facilitators in current care were investigated.

METHODS:
Eleven patients with knee OA were extensively interviewed using a semistructured script based on quality indicators. Directed content analysis, within the framework of Grol and Wensing, was performed to describe barriers and facilitators in 6 domains: guideline, health care professional, patient, social environment, organization, and financial context. Data were analyzed using NVIVO 10 software.

RESULTS:
In total, 38 barriers, at all 6 domains, were identified. The most frequently mentioned barriers were in the domains of the patient and the health care professional, namely, patients' disagreement with guidelines recommendations, negative experience with drugs, patients' limited comprehension of the disease process, and poor communication by the health care professional. The patients' disagreement with recommendations is further explained by the following barriers: "insistence on medical imaging," "fear that physiotherapy aggravates pain," and "perception that knee OA is not a priority health issue". Patients also reported 20 facilitators, all of which are listed as opposing barriers.

CONCLUSIONS:
Patients indicate that both personal factors and factors related to health care professionals play an important role in nonadherence. An interview script, based on quality indicators, was a significant aid to structurally formulate barriers and facilitators in the perceived knee OA care. Future guideline implementation strategies should take the identified barriers and facilitators into account.
Fiber helps


**Dietary intake of fiber in relation to knee pain trajectories.**

Dai Z¹, Lu N¹, Niu J¹, Felson DT¹, Zhang Y¹.

Objective Dietary fiber may reduce knee pain in part by lowering body weight and inflammation. In this study, we assessed whether fiber intake was associated with knee pain development patterns.

Methods In a prospective, multicenter cohort of 4,796 men and women aged 45-79 years with or at risk of knee osteoarthritis in Osteoarthritis Initiative, participants were followed up annually for 8 years. Dietary fiber was estimated using a validated food frequency questionnaire at baseline. Group-based trajectory modeling was used to identify WOMAC pain trajectories, which were assessed for the associations with dietary fiber intake using polytomous regression models.

Results Of the 4,470 eligible participants (8,940 knees) [mean age: 61.3 (SD: 9.1) years, 58% women], 4.9% underwent knee replacement and were censored at the time of surgery. Four distinct knee pain patterns were identified: no pain (34.5%), mild pain (38.1%), moderate pain (21.2%) and severe pain (6.2%). Dietary total fiber was inversely related to membership in the moderate or severe pain group (both p for trend ≤0.006). Subjects in the highest versus lowest quartile of total fiber had lower risks of belonging to moderate pain (OR=0.76, 95% CI: 0.61, 0.93) and severe pain patterns (OR=0.56, 95% CI: 0.41, 0.78). Similar results were found for grain fiber with these two pain patterns.

Conclusion Our findings suggest that high dietary total or grain fiber, particularly in the recommended daily fiber average intake of 25g per day, was associated with lower risks of belonging to moderate and severe knee pain development patterns over time. This article is protected by copyright. All rights reserved.
41 A. ACHILLES TENDON AND CALF

Comparisons of volleyball players


Elastographic Findings of Achilles Tendons in Asymptomatic Professional Male Volleyball Players.
Balaban M1, Idilman IS1, Ipek A2, Ikiz SS1, Bektaser B3, Gumus M1.

OBJECTIVES:
Elastography is a new sonographic technique that evaluates the elasticity of different tissues such as the Achilles tendon. In this study, we aimed to investigate the elastographic findings of Achilles tendons in professional athletes in comparison with healthy volunteers.

METHODS:
Twenty-one professional male volleyball players with no history of Achilles trauma were included in this study. Twenty-one healthy male volunteers with similar ages and body mass indices were selected as control participants. All participants underwent sonographic and elastographic evaluations of the Achilles tendons to evaluate Achilles tendon thickness and stiffness.

RESULTS:
We observed thickening in many of the thirds of the Achilles tendons (right proximal, right middle, left middle, and left distal thirds) of athletes in comparison with healthy volunteers. We did not detect any abnormalities according to the sonographic evaluations in both athletes and healthy volunteers. In the elastographic evaluations, we observed softening in the middle thirds of the Achilles tendons of athletes according to the main types (P < .001) and subtypes (P < .001 for right; and P = .002 for left middle third). There was no difference observed in the elastographic evaluations of the proximal and distal thirds.

CONCLUSIONS:
On sonography and elastography, we observed thickening and softening in Achilles tendons of athletes in comparison with healthy volunteers who had similar ages and body mass indices. These changes could be associated with early tendon degeneration. Further longitudinal studies may support this consideration.
44. RHUMATOID ARTHRITIS

Circadian rhythm changes


Dysregulated circadian rhythm pathway in human osteoarthritis: NR1D1 and BMAL1 suppression alters TGF-β signaling in chondrocytes.

Akagi R1, Akatsu Y1, Fisch KM2, Alvarez-Garcia O2, Teramura T2, Muramatsu Y2, Saito M3, Sasho T4, Su AI2, Lotz MK5.

OBJECTIVES:
Circadian rhythm (CR) was identified by RNA sequencing as the most dysregulated pathway in human osteoarthritis (OA) in articular cartilage. This study examined circadian rhythmicity in cultured chondrocytes and the role of the CR genes NR1D1 and BMAL1 in regulating chondrocyte functions.

METHODS:
RNA was extracted from normal and OA-affected human knee cartilage (n = 14 each). Expression levels of NR1D1 and BMAL1 mRNA and protein were assessed by quantitative PCR and immunohistochemistry. Human chondrocytes were synchronized and harvested at regular intervals to examine circadian rhythmicity in RNA and protein expression. Chondrocytes were treated with small interfering RNA (siRNA) for NR1D1 or BMAL1, followed by RNA sequencing and analysis of the effects on the TGF-β pathway.

RESULTS:
NR1D1 and BMAL1 mRNA and protein levels were significantly reduced in OA compared to normal cartilage. In cultured human chondrocytes, a clear circadian rhythmicity was observed for NR1D1 and BMAL1. Increased BMAL1 expression was observed after knocking down NR1D1, and decreased NR1D1 levels were observed after knocking down BMAL1. Sequencing of RNA from chondrocytes treated with NR1D1 or BMAL1 siRNA identified 330 and 68 significantly different genes, respectively, and this predominantly affected the TGF-β signaling pathway.

CONCLUSIONS:
The CR pathway is dysregulated in OA cartilage. Interference with circadian rhythmicity in cultured chondrocytes affects TGF-β signaling, which is a central pathway in cartilage homeostasis.
Comparisons of QOL


Health-related quality of life and utility: comparison of ankylosing spondylitis, rheumatoid arthritis, and systemic lupus erythematosus patients in Taiwan.

Chen HH1,2,3,4,5,6,7, Chen DY8,9,10,11,12,13, Chen YM8,9,10,11, Lai KL10,11.

The purpose of this study was to evaluate the health-related quality of life among patients with ankylosing spondylitis (AS), rheumatoid arthritis (RA), or systemic lupus erythematosus (SLE).

This prospective, cross-sectional survey was conducted from September 1, 2008 to August 31, 2009. Patients answered questions with regard to demographics and disease characteristics and also completed generic (SF-36) and preference-based utility (SF-6D and EQ-5D) instruments. Multivariate analysis assessed the relationship of RA and SLE to AS with respect to the outcomes of the different health-related quality of life instruments. In general, baseline and disease characteristics differed across the three disease groups. Compared to SLE patients, RA patients scored worse on the higher-order summary scores of physical (PCS) and mental components (MCS) of SF-36 (P ≤ 0.002) and total SF-36 (P ≤ 0.005). RA also had worse PCS than AS (P ≤ 0.001). SLE patients scored higher on the utility score of SF-6D compared with RA patients and higher than both AS and RA patients for the utility score of EQ-5D. Multivariate analysis found that compared with AS patients, RA had significantly lower SF-36 total score and PCS, and SLE patients had greater PCS and a greater EQ-5D utility score. Multivariate analysis found no difference across the patient groups with respect to MCS or SF-6D utility score.

These findings suggest that among the three rheumatic diseases studied, RA patients have the worse health-related quality of life, and AS patients have similar or poorer health-related quality of life as SLE patient.
Impact of spinal manipulation

Effect of lumbar spinal manipulation on local and remote pressure pain threshold and pinprick sensitivity in asymptomatic individuals: a randomised trial

- Sasha L. Dorro Barrett E. Losco, Peter D. Drummond and Bruce F. Walker

Chiropractic & Manual Therapies 2016 24:47

Background

The mechanisms of clinical pain relief associated with spinal manipulative therapy (SMT) are poorly understood. Our objective was to determine whether lumbar high-velocity low-amplitude SMT altered pressure pain threshold (PPT) and pinprick sensitivity (PPS) locally and remotely, how long any change lasted (up to 30 min), and whether changes related to the side of SMT.

Methods

Thirty-four asymptomatic participants (mean age 22.6 years ±4.0) received a right- or left-sided lumbar SMT. PPT and PPS were measured bilaterally at the calf, lumbar spine, scapula, and forehead before and immediately, 10, 20, and 30 min after intervention. Data were collected between October 2014 and June 2015.

Results

Bilateral calf and lumbar spine PPT increased significantly after 10 – 20 min and was maintained at 30 min (7.2–11.8 % increase). PPS decreased significantly in all locations at various times (9.8 – 22.5 % decrease). At the calf and lumbar spine, PPT increased slightly more ipsilateral to the SMT than contralateral.

Conclusions

Lumbar SMT reduced deep pressure sensitivity locally and in the lower limbs for at least 30 min, whereas sensitivity to pinprick was reduced systemically. These findings suggest that SMT specifically inhibits deep pressure sensitivity distally. These findings are novel compared to other lumbar SMT studies, and may reflect a local spinal or complex supraspinal analgesic mechanism.
45 D. MANUAL THERAPY EXTREMITIES

Knee MT helps


Treatment effectiveness and fidelity of manual therapy to the knee: A systematic review and meta-analysis.
Salamh P1, Cook C1, Reiman MP1, Sheets C2.

Manual therapy (MT) is a commonly used treatment for knee osteoarthritis (OA) but to date only one systematic review has explored its effectiveness.

The purpose of the present study was to perform a systematic review and meta-analysis of the literature, to determine the effectiveness and fidelity of studies using MT techniques in individuals with knee OA. Relevant studies were assessed for inclusion. Effectiveness was measured using effect sizes, and methodological bias and treatment fidelity were both explored. Effect sizes were calculated using standardized mean differences (SMD) based on pooled data depending on statistical and clinical heterogeneity, as well as risk of bias. The search captured 2,969 studies; after screening, 12 were included. Four had a low risk of bias and high treatment fidelity. For self-reported function, comparing MT with no treatment resulted in a large effect size (standardized mean difference [SMD] 0.84), as did adding MT to a comparator treatment (SMD 0.78). A significant difference was found for pain when adding MT to a comparator treatment (SMD 0.73).

The findings in the present meta-analytical review support the use of MT versus a number of different comparators for improvement in self-reported knee function. Lesser support is present for pain reduction, and no endorsement of functional performance can be made at this time.
52. EXERCISE

Deconditioned state and mortality

Interactive Effects of Aerobic Fitness, Strength, and Obesity on Mortality in Men.
Crump C\textsuperscript{1}, Sundquist J\textsuperscript{2}, Winkleby MA\textsuperscript{3}, Sundquist K\textsuperscript{2}.

**INTRODUCTION:**
Low aerobic fitness, low muscular strength, and obesity have been associated with premature mortality, but their interactive effects are unknown. This study examined interactions among these common, modifiable factors, to help inform more-effective preventive interventions.

**METHODS:**
This national cohort study included all 1,547,478 military conscripts in Sweden during 1969-1997 (97%-98% of all men aged 18 years each year). Aerobic fitness, muscular strength, and BMI measurements were examined in relation to all-cause and cardiovascular mortality through 2012 (maximum age, 62 years). Data were collected/analyzed in 2015-2016.

**RESULTS:**
Low aerobic fitness, low muscular strength, and obesity at age 18 years were independently associated with higher all-cause and cardiovascular mortality in adulthood. The combination of low aerobic fitness and muscular strength (lowest versus highest tertiles) was associated with twofold all-cause mortality (adjusted hazard ratio=2.01; 95% CI=1.93, 2.08; p<0.001; mortality rates per 100,000 person years, 247.2 vs 73.8), and 2.6-fold cardiovascular mortality (2.63; 95% CI=2.38, 2.91; p<0.001; 43.9 vs 8.3). These factors also had positive additive and multiplicative interactions in relation to all-cause mortality (their combined effect exceeded the sum or product of their separate effects; p<0.001), and were associated with higher mortality even among men with normal BMI.

**CONCLUSIONS:**
Low aerobic fitness, low muscular strength, and obesity at age 18 years were associated with increased mortality in adulthood, with interactive effects between aerobic fitness and muscular strength. Preventive interventions should begin early in life and include both aerobic fitness and muscular strength, even among those with normal BMI.
Exercise and depression

The roles of exercise and yoga in ameliorating depression as a risk factor for cognitive decline

Currently, there are no effective pharmaceutical treatments to reduce cognitive decline or prevent dementia.

At the same time, the global population is aging, and rates of dementia and mild cognitive impairment (MCI) are on the rise. As such, there is an increasing interest in complementary and alternative interventions to treat or reduce the risk of cognitive decline. Depression is one potentially modifiable risk factor for cognitive decline and dementia. Notably, exercise and yoga are two interventions known to both reduce symptoms of depression and improve cognitive function.

The current review discusses the efficacy of exercise and yoga to ameliorate depression and thereby reduce the risk of cognitive decline and potentially prevent dementia. Potential mechanisms of change, treatment implications, and future directions are discussed.
Tai Chi improvement in youth


Effects of tai chi chuan on anxiety and sleep quality in young adults: lessons from a randomized controlled feasibility study.
Caldwell KL1, Bergman SM2, Collier SR3, Triplett NT3, Quin R4, Bergquist J5, Pieper CF6

OBJECTIVE:
To determine feasibility and estimate the effect of a 10-week tai chi chuan (TCC) intervention on anxiety and sleep quality in young adults.

PARTICIPANTS:
Seventy-five adults (18-40 years) from a predominately undergraduate midsized university.

METHODS:
This was an assessor blinded, randomized feasibility trial, and participants were randomized into one of three groups: 10 weeks of TCC meeting 2 times per week, 10 weeks of TCC with a DVD of the curriculum, and control group receiving a handout on anxiety management. Anxiety and sleep quality were assessed 4 times: baseline, 4 weeks, 10 weeks (immediate post-intervention), and 2 months post-intervention. Retention was defined as a participant attending the baseline assessment and at least one other assessment. Adherence to the intervention was set a priori as attendance at 80% of the TCC classes.

RESULTS:
Eighty-five percent of participants were retained during the intervention and 70% completed the 2 month follow-up assessments. To increase statistical power, the two TCC groups were combined in the analyses of anxiety and sleep quality measures. No significant changes in anxiety were found in the control group, while levels of anxiety decreased significantly over time in the two TCC groups. Sleep quality scores improved across time for all three groups, but adherent TCC participants reported greater improvement than control participants.

CONCLUSION:
TCC may be an effective nonpharmaceutical means of improving anxiety and poor sleep quality in young adults.
Exercise and mental function


Impact of Exercise Intensity and Duration on Postexercise Executive Function.
Tsukamoto H¹, Takenaka S, Suga T, Tanaka D, Takeuchi T, Hamaoka T, Isaka T, Hashimoto T.

PURPOSE:
The impact of exercise volume represented by exercise intensity and duration on post-exercise executive function (EF) improvement remains unclear. In the present study, involving 2 volume-controlled evaluations, we aimed to compare acute exercise protocols with differing intensities and durations in order to establish an effective exercise protocol for improving EF.

METHODS:
In study 1, 12 healthy male subjects performed cycle ergometer exercise, based on a low-intensity (LI) protocol for 20 min (LI20), moderate-intensity (MI) protocol for 20 min (MI20), and MI20 volume-matched LI protocol for 40 min (LI40). The exercise intensities for the LI and MI were set at 30% and 60% of peak oxygen consumption, respectively. In study 2, 15 healthy male subjects performed MI exercise for 10 min (MI10), MI20, and 40 min (MI40). To evaluate the EF, the color-word Stroop task was administrated before exercise, immediately after exercise, and during the 30-min post-exercise recovery.

RESULTS:
In study 1, post-exercise EF improvement was sustained for a longer duration after MI20 than after LI40, and was sustained for a longer duration after LI40 than after LI20. In study 2, although there was no significant difference in post-MI exercise EF improvement, the magnitude of difference in the EF between the pre-exercise and 30-min post-exercise recovery period was moderately larger in MI40, but not in MI10 and MI20, indicating that the EF improvement during post-exercise recovery could be sustained after MI40.

CONCLUSION:
The present findings showed that post-exercise EF improvement could be prolonged after MI exercise with a moderate duration compared to volume-matched LI exercise with a longer duration. In addition, MI exercise with a relatively long duration may slightly prolong the post-exercise EF improvement.
Rumination pain and race


Pain-related Rumination, but not Magnification or Helplessness, Mediates Race and Sex Differences in Experimental Pain.

Meints SM¹, Stout M¹, Abplanalp S¹, Hirsh AT².

Compared to White individuals and men, Black individuals and women demonstrate a lower tolerance for experimental pain stimuli.

Previous studies suggest that pain catastrophizing is important in this context, but little is known about which components of catastrophizing contribute to these race and sex differences. The purpose of the current study was to examine the individual components of catastrophizing (rumination, magnification, and helplessness) as candidate mediators of race and sex differences in experimental pain tolerance. Healthy undergraduates (N=172, 74% female, 43.2% Black) participated in a cold pressor task and completed a situation-specific version of the Pain Catastrophizing Scale. Black and female participants demonstrated a lower pain tolerance than White (p<0.01; d=0.70) and male (p<0.01; d=0.55) participants, respectively. Multiple mediation analyses indicated that these race and sex differences were mediated by the rumination component of catastrophizing (indirect effect = -7.13 [95% CI: -16.20, -1.96] and 5.75 [95% CI: 0.81, 15.57], respectively) but not by the magnification (95% CI: -2.91, 3.65 and -1.54, 1.85, respectively) or helplessness (95% CI: -5.53, 3.31 and -0.72, 5.38, respectively) components. This study provides new information about race and sex differences in pain and suggests that treatments targeting the rumination component of catastrophizing may help mitigate pain-related disparities.

PERSPECTIVE:
This study suggests that differences in pain-related rumination, but not magnification or helplessness, are important contributors to race and sex differences in the pain experience. Interventions that target this maladaptive cognitive style may help reduce disparities in pain.
Pain modulation

Behavioral inhibition and behavioral activation are related to habituation of nociceptive flexion reflex, but not pain ratings

P.Maxwell Slepian Christopher R. France Lina K. Himawan Yvette M. Güereca Bethany L. Kuhn Shreela Palit

DOI: http://dx.doi.org/10.1016/j.jpain.2016.11.010

Highlights
- On average, pain ratings sensitize and NFR habituate to repeated noxious stimuli
- There is significant inter-individual variability in habituation of pain and NFR
- Behavioral inhibition is associated with attenuated habituation of NFR
- Behavioral activation is associated with enhanced habituation of NFR
- This study provides initial experimental support for the two-factor model of pain

Abstract
Habituation (i.e., decreases in responding) and sensitization (i.e., increases in responding) following prolonged or repeated exposures to a fixed stimulus, have been identified as important in adaptation to repeated or prolonged noxious stimulation. Determinants of habituation or sensitization are poorly understood, and experimental investigation of habituation of pain ratings have generally relied on pain reports and statistical techniques that average responses across a group of participants. Using a cross-sectional design, the current study employed multilevel growth curve analyses to examine changes in the nociceptive flexion reflex (NFR), a spinal nociceptive withdrawal reflex, and pain ratings in response to twelve repeated, constant-intensity, noxious electrocutaneous stimuli. Unconditional growth curve models indicated that, on average, participants evidenced habituation of the NFR and sensitization of pain ratings. However, a substantial subgroup of participants exhibited the opposite pattern of change. In conditional models, behavioral inhibition, b = 0.10, p=0.003 and behavioral activation, b = -0.07, p=0.07, independently interacted with the growth curve to predict changes in NFR, but not pain ratings, across the 12 stimuli. These findings provide preliminary experimental support for Jensen and colleagues’ (2016) two-factor model of pain experience and implicate a role for approach and avoidance motivations in descending modulation of NFR.

Perspective
Using repeated NFR stimulation, this study demonstrated that most participants exhibited NFR habituation and pain sensitization; however, a substantial subgroup showed an opposite pattern of pain habituation (25.0%) and NFR sensitization (31.4%). Further, NFR habituation was moderated by individual differences in behavioral activation and behavioral inhibition.
Phantom pain and exercise training

Phantom motor execution facilitated by machine learning and augmented reality as treatment for phantom limb pain: A single group, clinical trial in patients with chronic intractable phantom limb pain

The Lancet, 12/02/2016

OrtizCatalan M, et al.

For phantom limb pain, this study suggests potential value in the motor execution of the phantom limb as a treatment. Promotion of phantom motor execution aided by machine learning, augmented and virtual reality, and gaming is a non–invasive, non–pharmacological, and engaging treatment with no identified side–effects at present.

Methods

- The authors recruited patients with upper limb amputation and known chronic intractable phantom limb pain at 3 clinics in Sweden and 1 in Slovenia.
- For this study, patients received 12 sessions of phantom motor execution using machine learning, augmented and virtual reality, and serious gaming.
- They evaluated changes in intensity, frequency, duration, quality, and intrusion of phantom limb pain by the use of the numeric rating scale, the pain rating index, the weighted pain distribution scale, and a study-specific frequency scale before each session and at follow-up interviews 1, 3, and 6 months after the last session.
- They also monitored changes in medication and prostheses.
- Using descriptive statistics results are reported and analyzed by non-parametric tests.

Results

- The authors enrolled 14 patients with intractable chronic phantom limb pain for whom conventional treatments failed, between Sept 15, 2014, and April 10, 2015.
- Patients demonstrated statistically and clinically significant improvements in all metrics of phantom limb pain after 12 sessions.
- From pre-treatment to the last treatment session, phantom limb pain decreased by 47% (SD 39; absolute mean change 1·0 [0·8]; p=0·001) for weighted pain distribution, 32% (38; absolute mean change 1·6 [1·8]; p=0·007) for the numeric rating scale, and 51% (33; absolute mean change 9·6 [8·1]; p=0·0001) for the pain rating index.
- As per the outcomes, the numeric rating scale score for intrusion of phantom limb pain in activities of daily living and sleep was reduced by 43% (SD 37; absolute mean change 2·4 [2·3]; p=0·004) and 61% (39; absolute mean change 2·3 [1·8]; p=0·001), respectively.
- 2 of 4 patients who were on medication reduced their intake by 81% (absolute reduction 1300 mg, gabapentin) and 33% (absolute reduction 75 mg, pregabalin).
- The study reveals that improvements remained 6 months after the last treatment.
Knee pain and fiber


Dietary intake of fiber in relation to knee pain trajectories.
Dai Z1, Lu N1, Niu J1, Felson DT1, Zhang Y1.

Objective Dietary fiber may reduce knee pain in part by lowering body weight and inflammation. In this study, we assessed whether fiber intake was associated with knee pain development patterns.

Methods In a prospective, multicenter cohort of 4,796 men and women aged 45-79 years with or at risk of knee osteoarthritis in Osteoarthritis Initiative, participants were followed up annually for 8 years. Dietary fiber was estimated using a validated food frequency questionnaire at baseline. Group-based trajectory modeling was used to identify WOMAC pain trajectories, which were assessed for the associations with dietary fiber intake using polytomous regression models.

Results Of the 4,470 eligible participants (8,940 knees) [mean age: 61.3 (SD: 9.1) years, 58% women], 4.9% underwent knee replacement and were censored at the time of surgery. Four distinct knee pain patterns were identified: no pain (34.5%), mild pain (38.1%), moderate pain (21.2%) and severe pain (6.2%). Dietary total fiber was inversely related to membership in the moderate or severe pain group (both p for trend ≤0.006). Subjects in the highest versus lowest quartile of total fiber had lower risks of belonging to moderate pain (OR=0.76, 95% CI: 0.61, 0.93) and severe pain patterns (OR=0.56, 95% CI: 0.41, 0.78). Similar results were found for grain fiber with these two pain patterns.

Conclusion Our findings suggest that high dietary total or grain fiber, particularly in the recommended daily fiber average intake of 25g per day, was associated with lower risks of belonging to moderate and severe knee pain development patterns over time. This article is protected by copyright. All rights reserved.
Red meat and colon CA

J Gastroenterol. 2016 Dec 2.

**A critical overview on the biological and molecular features of red and processed meat in colorectal carcinogenesis.**

Jeyakumar A¹, Dissabandara L², Gopalan V³,⁴.

A recent investigation by the World Health Organisation (WHO) has found that the consumption of processed meat and potentially red meat promotes carcinogenesis and can increase the risk of colorectal cancer.

This literature review aims to summarise both the red and processed meat molecules associated with colorectal carcinogenesis and investigate their relationship with the pathogenic process of colorectal cancer. Literature relating to the carcinogenic effect of red and processed meat molecules was critically reviewed. There are multiple molecules present in red and processed meat with a potential carcinogenic effect on colorectal tissues. Processed meat is more carcinogenic compared to red meat because of the abundance of potent nitrosoyl-heme molecules that form N-nitroso compounds. Studies have also noted that other molecules such as polycyclic aromatic hydrocarbons and heterocyclic amines have potential mechanisms for the initiation of colorectal cancer pathogenesis.

The non-human sugar molecule N-glycolyneuraminic acid may account for the carcinogenic effects of pork despite its heme content being comparable to that of chicken. Red meat products, especially those that have been processed, have a wide variety of carcinogenic molecules known to increase the risk of colorectal cancer. Thus, the outcome of this review is consistent with the recent findings of WHO.
Neonatal vitamin D status and risk of multiple sclerosis: A population-based case-control study.

Nielsen NM¹, Munger KL², Koch-Henriksen N², Hougaard DM², Magyari M², Jørgensen KT², Lundqvist M², Simonsen J², Jess T², Cohen A², Stenager E², Ascherio A².

OBJECTIVE:
As previous research has suggested that exposure to vitamin D insufficiency in utero may have relevance for the risk of multiple sclerosis (MS), we aimed to examine the direct association between level of neonatal vitamin D and risk of MS.

METHODS:
We carried out a matched case-control study. Dried blood spots samples (DBSS) belonging to 521 patients with MS were identified in the Danish Newborn Screening Biobank. For every patient with MS, 1-2 controls with the same sex and birth date were retrieved from the Biobank (n = 972). Level of 25-hydroxyvitamin D (25[OH]D) in the DBSS was measured using liquid chromatography tandem mass spectroscopy. The association between different levels of 25(OH)D and risk of MS was evaluated by odds ratios (OR) calculated in conditional logistic regression models.

RESULTS:
We observed that lower levels of 25(OH)D in neonates were associated with an increased risk of MS. In the analysis by quintiles, MS risk was highest among individuals in the bottom quintile (<20.7 nmol/L) and lowest among those in the top quintile of 25(OH)D (≥48.9 nmol/L), with an OR for top vs bottom of 0.53 (95% confidence interval [CI] 0.36-0.78). In the analysis treating 25(OH)D as a continuous variable, a 25 nmol/L increase in neonatal 25(OH)D resulted in a 30% reduced risk of MS (OR 0.70, 95% CI 0.57-0.84).

CONCLUSION:
Low concentrations of neonatal vitamin D are associated with an increased risk of MS. In light of the high prevalence of vitamin D insufficiency among pregnant women, our observation may have importance for public health.
Carbohydrate inflammation and obesity


**Meal rich in carbohydrate, but not protein or fat, reveals adverse immunometabolic responses associated with obesity.**

Parvaresh Rizi E¹,², Baig S¹, Shabeer M¹, Teo Y¹, Mok SF³, Loh TP³, Magkos F⁴,⁵, Virtue S⁶, Vidal-Puig A⁶, Tai ES¹,²,⁷, Khoo CM¹,²,⁷, Toh SA⁸,⁹,¹⁰,¹¹.

**BACKGROUND:**
Obesity-related insulin resistance is linked to inflammation. Immunometabolic function differs between lean and obese subjects, but whether macronutrient composition of ingested meals affects these responses is not well known. We examined the effects of a single meal rich in fat, protein, or carbohydrate on immunometabolic responses.

**METHODS:**
Nine lean insulin sensitive (LIS) men and 9 obese insulin resistant (OIR) men ingested high-carbohydrate (HC), high-fat (HF) or high-protein (HP) mixed meals in random order. We assessed plasma glucose, insulin, and cytokine responses and cytokine gene expression in circulating mononuclear cells (MNC) at fasting and postprandial states (up to 6-h).

**RESULTS:**
Expression of NF-κB and TNFα genes were greater; whereas that of TGFβ and IL-6 genes were lower, in the OIR compared to the LIS individuals. The differences were significantly greater after the HC meal, but not after the HP or HF meal. Similar results were obtained for plasma concentrations of TNFα and IL-6.

**CONCLUSIONS:**
Our findings indicate that a single HC meal has a distinct adverse effect on immunometabolic responses in the OIR individuals. The cumulative effect of such adverse responses to meals rich in carbohydrate may predispose the OIR individuals to a higher risk of cardiovascular disease.
Cocoa intake


Habitual cocoa intake reduces arterial stiffness in postmenopausal women regardless of intake frequency: a randomized parallel-group study.
Okamoto T¹, Kobayashi R¹, Natsume M², Nakazato K¹.

Arterial stiffness is substantially higher in postmenopausal than in premenopausal women.

Daily cocoa intake has been shown to reduce central arterial stiffness in health adults, regardless of age; however, the effect of cocoa-intake frequency on arterial stiffness in postmenopausal women remains unclear. Therefore, the purpose of this study was to investigate the effects of cocoa-intake frequency on arterial stiffness in postmenopausal women. A total of 26 postmenopausal women (mean age ± standard deviation 64±12 years) were randomly assigned to two groups with different cocoa-intake frequencies: one group ingested 17 g of cocoa once daily except on Sundays (every-day group, n=13), and the other ingested 17 g of cocoa twice daily every other day (every-other-day group, n=13). These intake regimens were maintained in both groups for 12 weeks. Carotid-femoral pulse-wave velocity and femoral-ankle pulse-wave velocity were measured in both groups at baseline and again at the end of the 12-week study period. Compared to baseline, both pulse-wave velocities had significantly decreased after the 12-week study period in both groups (P<0.05). However, no significant difference in degree of change was observed between the two groups.

Although this study did not include a sedentary control group, these results suggest that regardless of frequency, habitual cocoa intake reduces central and peripheral arterial stiffness in postmenopausal women.
Vit D and E and gene expression


The effects of omega-3 fatty acids and vitamin E co-supplementation on gene expression of lipoprotein(a) and oxidized low-density lipoprotein, lipid profiles and biomarkers of oxidative stress in patients with polycystic ovary syndrome.

Rahmani E1, Samimi M2, Ebrahimim FA3, Foroozanfard F2, Ahmadi S3, Rahimi M4, Jamilian M5, Aghadavod E6, Bahmani F6, Taghizadeh M6, Memarzadeh MR7, Asemi Z8.

This study was conducted to determine the effects of omega-3 fatty acids and vitamin E co-supplementation on gene expression of lipoprotein(a) (Lp[a]) and oxidized low-density lipoprotein (Ox-LDL), lipid profiles and biomarkers of oxidative stress in women with polycystic ovary syndrome (PCOS).

This randomized double-blind, placebo-controlled trial was done on 68 women diagnosed with PCOS according to the Rotterdam criteria aged 18-40 years old. Participants were randomly assigned into two groups to receive either 1000 mg omega-3 fatty acids from flaxseed oil containing 400 mg α-Linolenic acid plus 400 IU vitamin E supplements (n = 34) or placebo (n = 34) for 12 weeks. Lp(a) and Ox-LDL mRNA levels were quantified in peripheral blood mononuclear cells of PCOS women with RT-PCR method. Lipid profiles and biomarkers of oxidative stress were quantified at the beginning of the study and after 12-week intervention. Quantitative results of RT-PCR demonstrated that compared with the placebo, omega-3 fatty acids and vitamin E co-supplementation downregulated expressed levels of Lp(a) mRNA (P < 0.001) and Ox-LDL mRNA (P < 0.001) in peripheral blood mononuclear cells of women with PCOS. In addition, compared to the placebo group, omega-3 fatty acids and vitamin E co-supplementation resulted in a significant decrease in serum triglycerides (-22.1 ± 22.3 vs. +7.7 ± 23.6 mg/dL, P < 0.001), VLDL- (-4.4 ± 4.5 vs. +1.5 ± 4.7 mg/dL, P < 0.001), total- (-20.3 ± 16.6 vs. +12.2 ± 26.1 mg/dL, P < 0.001), LDL- (-16.7 ± 15.3 vs. +11.9 ± 26.1 mg/dL, P < 0.001) and total/HDL-cholesterol (-0.5 ± 0.6 vs. +0.4 ± 0.8, P < 0.001). There were a significant increase in plasma total antioxidant capacity (+89.4 ± 108.9 vs. +5.9 ± 116.2 mmol/L, P = 0.003) and a significant decrease in malondialdehyde levels (-0.3 ± 0.4 vs. -0.008 ± 0.6 μmol/L, P = 0.01) by combined omega-3 fatty acids and vitamin E intake compared with the placebo group.

Overall, omega-3 fatty acids and vitamin E co-supplementation for 12 weeks in PCOS women significantly improved gene expression of Lp(a) and Ox-LDL, lipid profiles and biomarkers of oxidative stress.
Meat consumption in childhood

Prospective associations of meat consumption during childhood with measures of body composition during adolescence: results from the GINIplus and LISAplus birth cohorts

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Background

Higher meat and protein intakes have been associated with increased body weight in adults, but studies evaluating body composition are scarce. Furthermore, our knowledge in adolescents is limited. This study aimed to investigate the prospective associations of intakes of different meat types, and their respective protein contents during childhood, with body composition during adolescence.

Methods

Dietary (using food frequency questionnaires) and body composition (measured by bioelectrical impedance) data were collected from the 10- and 15-year follow-up assessments respectively, of the GINIplus and LISAplus birth cohort studies. Sex-stratified prospective associations of meat and meat protein intakes (total, processed, red meat and poultry) with fat mass index (FMI) and fat free mass index (FFMI), were assessed by linear regression models (N = 1610).

Results

Among males, higher poultry intakes at age 10 years were associated with a higher FMI at age 15 years [β = 0.278 (SE = 0.139), p = 0.046]; while higher intakes of total and red meat were prospectively associated with higher FFMI [0.386 (0.143), p = 0.007, and 0.333 (0.145), p = 0.022, respectively]. Additionally in males, protein was associated with FFMI for total and red meat [0.285 (0.145) and 0.356 (0.144), respectively].

Conclusions

Prospective associations of meat consumption with subsequent body composition in adolescents may differ by sex and meat source.
Pomegranate juice and BP


**Effects of pomegranate juice on blood pressure: A systematic review and meta-analysis of randomized controlled trials.**
Sahebkar A, Ferri C, Giorgini P, Bo S, Nachtigal P, Grassi D.

Punica granatum L. (Pomegranate) has been claimed to provide several health benefits. Pomegranate juice is a polyphenol-rich fruit juice with high antioxidant capacity. Several studies suggested that pomegranate juice can exert antiatherogenic, antioxidant, antihypertensive, and anti-inflammatory effects. Nevertheless, the potential cardioprotective benefits of pomegranate juice deserve further clinical investigation. To systematically review and meta-analyze available evidence from randomized placebo-controlled trials (RCTs) investigating the effects of pomegranate juice consumption and blood pressure (BP). A comprehensive literature search in Medline and Scopus was carried out to identify eligible RCTs. A meta-analysis of eligible studies was performed using a random-effects model. Quality assessment, sensitivity analysis, and publication bias evaluations were conducted using standard methods. Quantitative data synthesis from 8 RCTs showed significant reductions in both systolic [weighted mean difference (WMD): -4.96mmHg, 95% CI: -7.67 to -2.25, p<0.001] and diastolic BP (WMD: -2.01mmHg, 95% CI: -3.71 to -0.31, p=0.021) after pomegranate juice consumption. Effects on SBP remained stable to sensitivity analyses. Pomegranate juice reduced SBP regardless of the duration (>12 wks: WMD=-4.36mmHg, 95% CI: -7.89 to -0.82, p=0.016) and <12 wks: WMD=-5.83mmHg, 95% CI: -10.05 to -1.61, p=0.007) and dose consumed (>240cc: WMD=-3.62mmHg, 95% CI: -6.62 to -0.63, p=0.018) and <240cc: WMD=-11.01mmHg, 95% CI: -17.38 to -4.65, p=0.001, pomegranate juice per day) whereas doses >240cc provided a borderline significant effect in reducing DBP.

The present meta-analysis suggests consistent benefits of pomegranate juice consumption on BP. This evidence suggests it may be prudent to include this fruit juice in a heart-healthy diet.

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**KEYWORDS:** Antioxidants; Blood pressure; Cardiovascular risk; Flavonoids; Pomegranate
Omega 3’s fatty acids and vitamin E co-supplementation on gene expression of lipoprotein(a) and oxidized low-density lipoprotein, lipid profiles and biomarkers of oxidative stress in patients with polycystic ovary syndrome.

Rahmani E1, Samimi M2, Ebrahimi FA2, Foroozanfard F2, Ahmadi S3, Rahimi M4, Jamilian M5, Aghadavod E6, Bahmani F6, Taghizadeh M6, Memarzadeh MR7, Asemi Z8.

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