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PREFACE

Introduction

The library of the Central Council for Research in Homoeopathy has been circulating “Current Health Literature Awareness Service” (CHLAS). The main objective is to disseminate precise information/citation about scientific articles published in various journals/magazine subscribed by this Council.

Scope

This volume covers articles on AYUSH & other systems and Allied Sciences

Arrangement of Entries

The articles are indexed under the name of the authors, arranged in alphabetical order. The entries have been made in the following order:

Author
Title
Name of Journal
year of publication; Volume (issue no.): pagination
Abstract

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(Meenakshi Bhatia)
Librarian

Abstract:

Background: X-linked hypophosphataemia in children is characterised by elevated serum concentrations of fibroblast growth factor 23 (FGF23), hypophosphataemia, rickets, lower extremity bowing, and growth impairment. We compared the efficacy and safety of continuing conventional therapy, consisting of oral phosphate and active vitamin D, versus switching to burosumab, a fully human monoclonal antibody against FGF23, in paediatric X-linked hypophosphataemia.

Methods: In this randomised, active-controlled, open-label, phase 3 trial at 16 clinical sites, we enrolled children with X-linked hypophosphataemia aged 1–12 years. Key eligibility criteria were a total Thacher rickets severity score of at least 2·0, fasting serum phosphorus lower than 0·97 mmol/L (3·0 mg/dL), confirmed \textit{PHEX} (phosphate-regulating endopeptidase homolog, X-linked) mutation or variant of unknown significance in the patient or a family member with appropriate X-linked dominant inheritance, and receipt of conventional therapy for at least 6 consecutive months for children younger than 3 years or at least 12 consecutive months for children older than 3 years. Eligible patients were randomly assigned (1:1) to receive either subcutaneous burosumab starting at 0·8 mg/kg every 2 weeks (burosumab group) or conventional therapy prescribed by investigators (conventional therapy group). Both interventions lasted 64 weeks. The primary endpoint was change in rickets severity at week 40, assessed by the Radiographic Global Impression of Change global score. All patients who received at least one dose of treatment were included in the primary and safety analyses. The trial is registered with ClinicalTrials.gov, number NCT02915705.

Findings: Recruitment took place between Aug 3, 2016, and May 8, 2017. Of 122 patients assessed, 61 were enrolled. Of these, 32 (18 girls, 14 boys) were randomly assigned to continue receiving conventional therapy and 29 (16 girls, 13 boys) to receive burosumab. For the primary endpoint at week 40, patients in the burosumab group had significantly greater improvement in Radiographic Global Impression of Change global score than did patients in the conventional therapy group (least squares mean +1·9 [SE 0·1] with burosumab vs +0·8 [0·1] with conventional therapy; difference 1·1, 95% CI 0·8–1·5; p<0·0001). Treatment-emergent adverse events considered possibly, probably, or definitely related to treatment by the investigator occurred more frequently with burosumab (17 [59%] of 29 patients in the burosumab group vs seven [22%] of 32 patients in the conventional therapy group). Three serious adverse events occurred in each group, all considered unrelated to treatment and resolved.
**Interpretation:** Significantly greater clinical improvements were shown in rickets severity, growth, and biochemistries among children with X-linked hypophosphataemia treated with burosumab compared with those continuing conventional therapy.

**Funding:** Ultragenyx Pharmaceutical and Kyowa Kirin International.


**Abstract:**

Delusion is an idiosyncratic belief which is false but firm. It can be possibly a feature of Schizophrenia and maniac disorders psychosis. Allied Sciences has limited scope in treating it and generally causes long tormenting condition of patient. Homoeopathy being treated individually helps in tackling delusions and approaches the patient on its inner sphere and relives symptoms. In this article a case study is given of a patient managed with Hyoscyamus.


**Abstract:**

**Introduction:** Osteoarthritis (OA) is one of the most common and fast-growing chronic diseases among older adults. The aim of this study was to assess the effect of acupressure therapy on pain, stiffness, and physical functioning of a knee affected by osteoarthritis.

**Methods:** A single-blind pilot randomized control trial was conducted on 51 older adults with OA of the knee living in one of 3 nursing homes. Nursing homes were randomly allocated to one of three study groups; acupressure therapy, placebo, and routine care. The intervention group received acupressure therapy on eight acupoints. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total score and the separate WOMAC subscales were used to evaluate pain, stiffness and physical functioning of knees.

**Results:** A one-way ANOVA revealed that WOMAC index was not significantly different at the baseline between the three groups (P = 0.296). After intervention, ANOVA showed significant differences between groups in regard to total WOMAC index, pain and physical dysfunction (p < 0.001). Post hoc comparisons revealed that participants receiving acupressure showed a significant decrease in total WOMAC index, pain and physical dysfunction (p < 0.001). Indeed ANCOVA detected a difference in means of pain (p ≤ 0.001), stiffness (p = 0.038) and physical dysfunction (p ≤ 0.001) in three groups.
Conclusion: Acupressure may be an effective intervention for reducing the pain, stiffness, and improving the function of knees with osteoarthritis. Akhter Javed. There is no cure of this disease except Homoeopathic. National Journal of Homoeopathy 2019: 21 (6) 237th; 35-36p.

Abstract:

This case demonstrate the mindset of an individual, Focus about their concern, reaction and adaptation. On the basis of CAR feel the patient mind state then convert into rubric and reach the similimum.


Abstract:

Objective: The purpose of this study was to compare and evaluate the effects of occlusal splint and low dose laser treatments clinically and thermographically in patients with myofascial pain syndrome.

Methods: Twenty patients aged 18–45 with myofascial pain syndrome were involved into this study. Patients were examined by clinically and Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) was used for the diagnosis of TMD. Patients divided into two groups. First group treated with stabilisation splint, while the other one with low level laser therapy (LLLT). Pre- and post-treatment pain intensity, muscle sensitivity and the superficial skin temperature differences over the masseter and anterior temporal muscle were assessed, and comparison was made within and between the groups pre- and post-operatively.

Results: In both groups, there was a significant decrease in temperature values, especially in the masseter region (p < 0.05) and post-treatment pain intensity and muscle sensitivity values were lower than the pre-treatment values (p < 0.05). In addition, the heat values in certain regions of the masseter were lower in the LLLT group than in the splint group and there was a statistical difference in these regions between two groups (p < 0.05). However, there was no statistical difference in the pain intensity and muscle sensitivity between both groups (p > 0.05).

Conclusion: It was concluded that both occlusal splint therapy and low level laser therapy were effective in the treatment of MPS, and when thermographic data were taken into account, LLLT treatments could provide more advantageous results in these patients.


Abstract:

Hamilton (1978) defined delusion as ‘A false, unshakeable belief which arises from internal morbid processes. It is easily recognizable when it is out of
keeping with the person’s educational and cultural background.’

Psychodynamic theory by Freud (1911) proposed that delusion formation involve denial, contradiction and projection of repressed homosexual impulses that break out from the unconscious. Learning theorists have tried to explain delusions in terms of avoidance response, arising specially from fear of interpersonal encounter. All these theories explain delusions are feelings not based on facts. But they are from unconscious of individual the same for dreams. Dreams are reflection of individuals subconscious mind. The following case explains how important these feelings (delusions/dreams) are and how it helps us to find the right remedy.


Abstract:

Introduction: Human Herpes Virus-3 (Varicella Zoster Virus) causes Chickenpox in childhood and reactivates after decades of being latent to cause Herpes Zoster in adults. The aim of this study was to evaluate the in vitro antiviral potency on the leaves of Punica granatum L., Momordica charantia L., Andrographis paniculata Nees. and Melia azedarach L., against the Human Herpes Virus-3 isolated from Chickenpox and Zoster in comparison with acyclovir.

Methods: Aqueous, ethanolic and aqueous ethanolic extracts were prepared from the chosen plant leaves by lyophilization process and subjected to in vitro cytotoxicity assay in HEp-2 cells followed by the in vitro antiviral evaluation against the clinical isolates of HHV-3 using post incubation assay. The structure of leaf chemicals were retrieved from protein data bank and in silico drug analysis was carried out through discovery studio targeting the protease of HHV-3. The drug likeliness and the ADMETSAR properties of the screened active phytochemicals were calculated.

Results: Aqueous extract from the leaves of Punica granatum L., exhibited potential antiviral activity against the HHV-3. The in silico docking results found that the phytochemicals of Punica granatum L., interacted on the active site of the HHV-3 protease.

Conclusion: Aqueous extract from the leaves of Punica granatum L. was superior in exhibiting its antiviral efficacy to HHV-3 whose in vitro activity was comparable with acyclovir. As the leaf phytochemicals interacted with the HHV-3 protease, the antiviral activity of the Punica granatum L., leaves may interfere with the capsid assembly of the HHV-3.

Abstract:

A delusion is a false belief held by a person. It contradicts reality or what is commonly considered true. The strength of a delusion is based on how much the person believes it. Specifically, a delusion of grandeur is a person’s belief that they are someone other than who they are, such as a supernatural figure or a celebrity. A delusion of grandeur may also be a belief that they have special abilities, possessions or powers.


Abstract:

Introduction: Malaria is one of the most common major health problems in tropical low- and middle-income countries, with antimalarial drugs being highly effective but also threatened by increasing drug resistance. Clinically efficacious, well-tolerated antimalarial plants could be an important alternative treatment. This systematic review aims at identifying and critically appraising clinical trials testing plants with antimalarial properties for malaria treatment and/or prophylaxis.

Methods: Studies were identified through PubMed, Elsevier Scopus and Cochrane Central, and scanning article reference lists. Records were published in English between 01/01/2005 and 15/01/2018. A framework for analysis based on the CONSORT statement was used for data extraction. Risk of bias was assessed. A meta-analysis could not be conducted due to data heterogeneity.

Results: Nine studies met inclusion criteria. Extracts from Argemone mexicana, Artemisia annua, Citrus aurantifolia, Nauclea pobeguinii, Nycthanthes arbor-tristis and Vernonia amygdalina were examined. Methodological rigorosity varied. Adequate clinical response on day 14 with A. mexicana was 81% (p = 0.027) in one study and 89% (95% CI 84.1–93.2) on day 28 in another study. Similarly, 87.9% of participants taking N. pobeguinii had an adequate clinical response on day 14 (p = 0.003). The risk of bias and study quality varied. Two studies had a Jadad score of 3 and all others but one had a score of 1. All herbal preparations were safe with no moderate or severe adverse events being reported.

Conclusions: Studies have demonstrated that antimalarial plants show promise for malaria treatment and prophylaxis. A. mexicana and N. pobeguinii extracts were supported by the best evidence. More work should be undertaken to better understand relevant approaches.

Arikan Fatma, Uçar Mürvet Artuk, Kondak Yasemin, Tekeli Aysel et al. Reasons for complementary therapy use by cancer patients, information

Abstract:

**Background:** Cancer patients are known to commonly use complementary therapies (CT). However, it is emphasized that patients do not share sufficient information with health professionals about this subject and that the subject is ignored in oncology practice. The aim of the study is to assess cancer patients’ reasons for using complementary therapy, information resources and communication with health professionals.

**Methods:** The study is a descriptive, cross-sectional study. In this study, a questionnaire was used by the researchers. A questionnaire form consisting of 3 parts was used. In the first part of this form, there were questions about the gender, age and educational status of the patients (8 questions). In the second part, there were questions about disease and treatment information (3 questions), and the third part had questions about the use of complementary therapies (9 questions). To determine the use of complementary therapy, patients were asked ‘Do you currently use complementary treatment?’ (Yes or No). 183 patients included in the study completed the questionnaire about complementary therapies.

**Results:** In this study, it was determined that 37.7% of the patients were using complementary therapies. The most commonly used complementary therapy was natural products (46.4%). The most common reason for using complementary therapy was to provide support for treatment. Almost half of the cancer patients (48.5%) did not talk about this issue with their physicians, and 41.1% of them did not talk about CT with their nurses. The study found that the most important reason why the patients did not talk about CT was that they were not asked about it by health professionals.

**Conclusion:** This study determined that almost half of patients could not receive information about CT from health professionals. Patients expect physicians and nurses to initiate communication on this subject. Providing healthcare professionals with evidence-based counseling about CT is essential for improving patient safety and patient outcomes.


Abstract:

**Background:** Intentional Touch (InTouch) refers to a soft physical touch with the aim to ease complaints and enhance well-being. Central questions were perception of InTouch by nurses and patients and possible effects on pain perception.

**Patients and Methods:** InTouch was developed by stakeholder involvement. Nurses working in geriatric care received expert training in InTouch. Semi-
structured interviews and participant observation (including video recording) were conducted with nurses applying and patients with chronic pain receiving InTouch after the beginning of the intervention and after 4 weeks. Interviews were analyzed based on Qualitative Content Analysis and video recordings based on Qualitative Visual Analysis.

**Results:** Six elderly patients with chronic pain and 6 nurses were included. Nurses and patients equally described relaxation, well-being, and a sensation of warmth during the intervention. Patients reported no pain during the intervention. After the intervention, 3 patients each experienced pain relief or no change. Patients described better drive and positive feelings, and nurses felt empowered in their nursing work. Empathetic attention had special importance for improving the therapeutic relationship.

**Conclusion:** The results of this study suggest that InTouch promoted relaxation, well-being, and pain relief for elderly people suffering from chronic pain and may contribute positively to the therapeutic relationship.

**Baig Mirza Answer.** Ganga-jal can be a remedy for Alzheimer’s disease. *National Journal of Homoeopathy 2019: 21 (6) 237th; 44-45p*


**Abstract:**

Dental hygiene procedures are the primary steps to prevent and treat oral microbial diseases such as tooth decay and periodontitis. However, these procedures can be psychologically difficult for patients to face. It is normal to feel some discomfort during these procedures, although this can sometimes cause patients to avoid dental hygiene procedures, starting a negative cycle and leading to the accumulation of tartar and the increase of microbial load in the oral cavity. Therefore, it is prudent to consider the application of natural extracts with healing and relieving properties after air-polishing procedures. This commentary discusses complementary herbal medicine applied in the dental field, which could be used in the treatment of dental patients.


**Abstract:**

**Introduction:** Medicinal cannabis has been used for over 6000 years. It may be accessed legally in many western countries, yet in Australia, access is very difficult. It is treated as a pharmaceutical and an ‘unapproved therapeutic good’ and is subsequently subject to a complex regulatory system around prescribing. There have been calls by authoritative bodies in Australia for more evidence in relation to its efficacy and safety, suggesting that this is
inadequate. The adoption of the evidence-based medicine (EBM) approach as the basis of decision-making in the healthcare sector positions systematic reviews and randomised controlled trials (RCTs) at the top of the hierarchy of evidence. It is largely this form of evidence that has been used to argue for or against the efficacy and safety of cannabis and to substantiate the current regulatory system in Australia. It is therefore important to understand the EBM approach and factors that need to be considered when examining scientific research into cannabis, in order to decide whether there is sufficient evidence or not. It is argued that regulation of cannabis is inappropriate, based on a limited understanding of evidence, and continues to limit access to medicinal cannabis by patients.

Methods: This paper examines the notion of evidence in medicine, points of consideration in scrutinizing research methodology, what the actual evidence is in relation to safety and efficacy of medicinal cannabis, the implications of evidence and whether it supports the current regulatory framework around medicinal cannabis in Australia. It poses an alternative regulatory approach.

Results: A robust definition of EBM goes beyond the notion of simply scientific evidence in the form of RCTs and systematic reviews. Rigorous scrutiny of the evidence about cannabis is required, since evidence is being used to control access. Scientific evidence including reports from authoritative bodies indicates there is much evidence to support the safety and efficacy of medicinal cannabis. CBD has been found to be relatively safe, non-addictive and efficacious. Access to medicines that alleviate suffering in a timely manner is a human right and a medical responsibility. There is enough evidence to justify regulatory changes to significantly increase access to medicinal cannabis in Australia.

Conclusion: We need to bring back the human element when considering what evidence we use and how we use it in medicine. Cannabis has the potential to alleviate much suffering, and patient (human) rights must be central in public policy. There is already much scientific evidence in relation to safety and efficacy of cannabis and cannabinoids such as CBD and THC. In Australia, the current regulatory system needs to be disbanded, cannabis products treated as ‘approved goods’ and regulated as complementary medicines (for products containing CBD and low THC) or in the case of high THC-containing products, regulated under the SUSMP as an S4 (rather than S8) medicine.


Abstract:
**Background:** Polycystic ovary syndrome (PCOS) is a common and heterogeneous endocrine disorder in reproductive-age women. Tung’s acupuncture, a Traditional Chinese Medicine (TCM) treatment, is widely used for PCOS in East Asia, but evidence on its efficacy is rare. The aim of this RCT study was to examine whether the Tung’s acupuncture could be a complementary treatment method for PCOS.

**Methods:** A total of 60 PCOS patients were randomly assigned to a Tung’s acupuncture group (n = 30) or a cyproterone acetate/ethinylestradiol (CPA/EE) group (n = 30). Each participant received treatments for 12 weeks to assess the short-term treatment efficacy and then followed up for another 12 weeks to assess the long-term treatment efficacy. The primary outcome examined was change in the ratio of luteinizing hormone (LH) to follicle-stimulating hormone (FSH); the secondary outcomes examined were changes in body mass index (BMI), LH, FSH, total testosterone (TT), ovarian volume, polycystic ovary number and menstrual frequency.

**Results:** Both groups showed significant reductions in the LH/FSH ratio, LH and TT after 12-week treatment (p < 0.001) and 12-week follow-up (p < 0.05). No significant differences existed between the two groups (p > 0.05). Both groups showed significant improvement in BMI, menstrual frequency and polycystic ovary number after 12-week treatment (p < 0.05).

**Conclusion:** Compared with CPA/EE, Tung’s acupuncture showed no better improvement on LH/FSH ratio for PCOS although it could reduce the ratio. Tung’s acupuncture might have some effect on long-term weight control and menstruation frequency. Further studies addressing this study’s limitations are recommended.


**Abstract:**

**Objectives:** To determine the short-term effects of a modified Flexion-Distraction (FD) technique in comparison with a high-velocity low-back spinal manipulation (HVLA-SM) protocol on patients suffering from chronic low-back pain (CLBP).

**Design and methods:** A randomized controlled trial. The sample was composed of 150 patients suffering from CLBP, who were randomly assigned to either a FD (n = 75) or a HVLA-SM (n = 75) group. The variables used to study pain were the scores of the Visual Analogue Scale (VAS) and the Pressure Pain Threshold (PPT) on trigger points (TrPs) of the quadratus lumborum. In addition, the Oswestry Disability Index (ODI) was used to measure disability,
and Schober’s test and the Finger Floor Distance test (FFDT) to measure changes in low-back spine motion. An Analysis of Covariance (ANCOVA) was used to measure group effect, and Number Needed to Treat (NNT) for effect size.

**Results:** Greater improvements occurred in the FD group, with a statistically significant group effect ($p < 0.001$) for all outcome variables. The $\eta^2$ value was larger than 0.100 in the Schober’s and FDD tests, larger than 0.200 in the case of ODI and PPT, and larger than 0.300 for VAS. $\text{OR} = 0.07$ ($\text{IC 95%} = 0.03$ to $0.18$) and $\text{NNT} = 2.08$ ($\text{IC 95%} = 1.64$–$2.84$) yielded improved values for the FD group.

**Conclusion:** For patients suffering from CLBP, greater improvements in pain and function were observed in the group receiving the modified FD treatment than in the HVLA-SM group.


**Abstract:**

**Purpose:** The purpose of this review is to identify how an interdisciplinary collaborative effort between occupational therapists, speech language pathologists, and physical therapists can promote mindfulness to alleviate boredom in school-age children.

**Methods:** A review of literature was utilized to meet four objectives: establish sources of boredom, distinguish between occupational deprivation and excessive opportunities, delve specifically into the societal aspects of boredom occurring in the United States, and make recommendations for a multidisciplinary approach to boredom. Four articles met the inclusion criteria.

**Results:** Boredom is thought to be the result of personal factors including personality, difficulty with attending, and negative attitudes. It can be the result of both excessive opportunities and deprivation. Boredom can have lifelong negative impacts. A multidisciplinary team is ideal for implementing mindfulness into practice.

**Conclusion:** Rehabilitation professionals are in a unique position to facilitate mindfulness to eliminate boredom and create life balance, by cultivating the core building blocks of intention, attention, and a mindful way attitude.


**Abstract:**

**Background:** It is well known that massage therapists routinely develop a number of health problems related to their profession.

**Purpose:** To determine the effects of grounding on massage therapists’ quality of life and pain. Grounding refers to being in direct body contact with the ground, such as walking barefoot on humid soil or on grass.

**Setting:** The Chopra Center for Well-Being in Carlsbad, California, USA.

**Participants:** Sixteen massage therapists (mean age 42.8 years).

**Research design and intervention:** A stepped wedge cluster design was incorporated into a 6-week double-blind Randomized Controlled Trial (RCT) procedure with massage therapists assigned randomly into one of two cohorts. Therapists were not grounded for the first week, were grounded while working on clients and at home while sleeping for the next four weeks, and then ungrounded for the last week.

**Outcome measures:** Prior to, during, and immediately following the intervention, participants completed standardized questionnaires reporting on pain, physical function, anxiety, depression, fatigue/tiredness, sleep disturbance and number of hours of sleep, number of clients worked on per working day, energy, and emotional and mental stress.

**Results:** As a group, therapists experienced significant increases in physical function and energy and significant decreases in fatigue, depressed mood, tiredness and pain while grounded as compared to not being grounded. At one-month following the study, physical function was also increased and depressed mood and fatigue were decreased.

**Conclusions:** We observed consistent beneficial effects of grounding in domains highly relevant to massage therapists, namely pain, physical function, and mood. These findings, combined with prior results from this trial indicating improvements in inflammatory biomarkers, blood viscosity and heart rate variability (HRV), suggest that grounding is beneficial to massage therapists in multiple domains relevant to their occupation, supporting overall health and quality of life.


**Abstract:**
Increasing awareness about the after effects of analgesic and antispasmodic drugs in the public can lead more people to prefer homoeopathic treatment for dysmenorrhea. The analgesic drugs gives only temporary relief and it is not a complete solution for those who suffer from dysmenorrhea. Homoeopaths who have sound knowledge in therapeutics can be able to give a permanent cure for dysmenorrhoea.

Darand Mina, Darabi Zahra, Yari Zahra, Saadati Saeedeh et al. *Nigella sativa* and inflammatory biomarkers in patients with non-alcoholic fatty liver disease: Results from a randomized, double-blind, placebo-controlled, clinical trial. *Complementary Therapies in Medicine* 2019; 44:196-03p

**Abstract:**

**Objective:** The aim of this study was to assess the effects of *Nigella sativa* consumption on inflammatory biomarkers in patients with Non-alcoholic fatty liver disease (NAFLD).

**Methods:** This is a randomized, double-blind, placebo-controlled clinical trial. Fifty NAFLD patients were assigned to receive either two gram/day *Nigella sativa* seed as *Nigella sativa* group (NSG), or two gram/day starch as placebo group (PG) for 12 weeks.

**Results:** At the end of the study, the serum levels of tumor necrosis factor-α (TNF-α) decreased significantly compared with the beginning of the study in both groups, while the levels of high sensitive C reactive protein (hs-CRP) and nuclear factor kappa-B (NF-κB) only decreased significantly in the NSG (P < 0.05). Only reduction in the serum levels of TNF-α was significantly more in NSG compared to the PG (P = 0.001). After adjusting the effects of confounding factors, the results remained unchanged. According to Fibroscan exam, hepatic steatosis and its percentage decreased significantly only in the NSG (P < 0.005); however, the changes were not significantly different between two groups. After adjusting for confounding factors, only steatosis percentage reduction was significantly more in the NSG compared to PG (P = 0.005).

**Conclusion:** Our results have shown that two gram/day consumption of *Nigella sativa* can reduce inflammatory biomarkers in patients with NAFLD. Further studies with different doses are highly recommended to find the optimal dosage.


**Abstract:**

**Background:** Echinacea preparations are commonly used to prevent and treat upper respiratory tract infection.
**Objective:** To assess current evidence for the safety and efficacy of echinacea containing preparations in preventing and treating upper respiratory tract infection.

**Data source:** MEDLINE, EMBASE, CAB extracts, Web of Science, Cochrane DARE, clinicaltrials.gov and the WHO ICTRP – 1980 to present day.

**Eligibility criteria:** Randomised double-blind placebo-controlled trials using an echinacea preparation to prevent or treat upper respiratory tract infections.

**Participants and interventions:** Participants who are otherwise healthy of any age and sex. We considered any echinacea containing preparation.

**Study appraisal and synthesis methods:** We used the Cochrane collaborations tool for quality assessment of included studies and performed three meta-analyses; on the prevention, duration and safety of echinacea.

**Results:** For the prevention of upper respiratory tract infection using echinacea we found a risk ratio of 0.78 [95% CI 0.68–0.88], for the treatment of upper respiratory tract infection using echinacea we found a mean difference in average duration of −0.45 [95% 1.85–0.94] days, finally for the safety meta-analyses we found a risk ratio of 1.09 [95% CI 0.95–1.25].

**Limitations:** The limitations of our review include the clinical heterogeneity – for example many different preparations were tested, the risk of selective reporting, deviations from our protocol and lack of contact with study authors.

**Conclusions:** Our review presents evidence that echinacea might have a preventative effect on the incidence of upper respiratory tract infections but whether this effect is clinically meaningful is debatable. We did not find any evidence for an effect on the duration of upper respiratory tract infections. Regarding the safety of echinacea no risk is apparent in the short term at least. The strength of these conclusions is limited by the risk of selective reporting and methodological heterogeneity.

**Implications of key findings:** Based on the results of this review users of echinacea can be assured that echinacea preparations are safe to consume in the short term however they should not be confident that commercially available remedies are likely to shorten the duration or effectively prevent URTI. Researchers interested in the potential preventative effects of echinacea identified in this study should aim to increase the methodological strength of any further trials.

**Dehkordi Z. Raisi, Rafieian-kopaei M., Hosseini-Baharanchi F.S. A double-blind controlled crossover study to investigate the efficacy of salix extract on primary dysmenorrhea. Complementary Therapies in Medicine 2019; 44:102-09p.**

**Abstract:**
Objectives: Primary dysmenorrhea in the absence of pelvic pathology is a common gynecologic disorder affecting the quality of life of women of reproductive age. This study evaluates the effect of salix extract on primary dysmenorrhea.

Design: This study was a randomized crossover clinical trial.

Setting: The study population included 96 female students with level two or three of primary dysmenorrhea: 48 students in the treatment group (sequence I) followed by control (sequence II) and 48 students in control group (sequence I) followed by treatment (sequence II).

Interventions: The intervention was salix capsule (400 mg daily) and the active control was mefenamic acid capsule (750 mg daily) as.

Main outcomes: Pain intensity, measured by the visual analog scale (VAS), amount of bleeding, and severity of dysmenorrhea symptoms were outcomes. Generalized estimating equations were used for data analysis.

Results: The demographic and menstrual characteristics of the students were homogenous between the groups. The results showed that the students in mefenamic acid group had a significantly higher level of VAS than the students in the salix group over time (1.61 ± 0.06, P < 0.001). The estimated odds of the bleeding level in the salix and mefenamic acid group were not significantly different (P = 0.31). In average, 77.39%±16.18 of the students in salix group showed no symptoms followed by 22.18%±14.08 of the students who experienced mild symptoms. Averagely, 44.58%±20.16 of the students in the mefenamic acid group had mild symptoms followed by moderate symptoms (28.12%±15.29).

Conclusions: Salix extract significantly decreased dysmenorrhea in comparison to mefenamic acid, as the standard treatment of dysmenorrhea.


Abstract:

Background: Mild cognitive impairment (MCI) prevalence is estimated at 6%-12% of the population. It is possible that early treatment at the MCI stage could reduce progression to more severe cognitive impairment. The Montreal Cognitive Assessment (MoCA) is a sensitive measure used to assess changes in cognitive function. Various Chinese herbal medicines (CHMs) have been tested for effects on MCI using MoCA.

Objectives: To evaluate the clinical evidence for CHMs on MoCA scores in MCI.
**Design:** Five biomedical databases in English and Chinese language were searched for randomized controlled trials that compared orally administered CHMs with a control group and assessed changes in cognition using MoCA. Analyses were based on the comparison, control intervention, and study duration. Mean differences and 95% confidence intervals were calculated to evaluate treatment effects. For each study, risk of bias was assessed according to the Cochrane tool.

**Results:** Nineteen studies were included with 16 contributing to the data analyses. Three studies were placebo controlled. Nine compared a CHM with a pharmacotherapy, three combined a CHM with a pharmacotherapy, and one combined CHM with cognitive training. In the two placebo-controlled studies of 24-week duration, results favored the CHMs at end of treatment.

**Forseth Bethany, Boyer William, Miller Amy , Fitzhugh Eugene C. et al.**


**Abstract:**

**Objective:** To examine and compare the demographic, health behavior, and cardiometabolic risk factor characteristics of participants who report 1) participating in yoga, 2) not participating yoga, or 3) are inactive, using a nationally representative sample of U.S. adults.

**Design:** Study participants were from the 1999–2006 National Health and Nutrition Examination Survey (NHANES) who self-reported participation in yoga (n = 74), no-yoga (n = 3,753) or were inactive (n = 1,285).Participants in the no-yoga group did engage in other types of physical activity, while the inactive group reported no activity during the survey period.

**Results:** Yoga participants were primarily female (80.7%), college educated (51.9%), mostly non-smokers (46.9%), and reported moderate alcohol consumption (72.1%). Yoga participants were found to be significantly less likely to have an elevated waist circumference (OR = 0.40, p < 0.01; OR = 0.30, p < 0.01), and a low HDL (OR = 0.43, p = 0.03; OR = 0.34, p < 0.05) compared to both non-yoga participants and inactive individuals, respectively. Yoga participants were 61% less likely to have elevated blood glucose compared to non-yoga participants (OR = 0.39, p < 0.05). Compared to inactive individuals, yoga participants were 52% (OR = 0.48, p < 0.05) and 66% (OR = 0.34, p < 0.05) less likely have an elevated body mass index and have elevated triglyceride levels, respectively.

**Conclusions:** Given the emergence of yoga as a common form of physical activity, it is imperative to understand the characteristics of those who participate in yoga to further understand its relationship with cardiovascular risk. This study was one of the first to use nationally-representative data and objectively measured cardiometabolic variables.


Abstract:

**Introduction:** Movement orientated Mind-Body-Interventions become more popular. But there are no standardized documentation tools to show if an improvement in movement could correlate with an improvement in health. Yet systematic documentation is a vital requirement to their efficacy.

**Method:** We developed a 5-module documentation structure including patients’ perspective. Over a period of five months 11 therapists used the modules to document their treatments on 41 patients and evaluated their feasibility at hand a questionnaire.

**Results:** 10 therapists and 37 patients met the inclusion criteria. In a documented variety of treatment concepts moderate to large effect size in observed movement qualities was found. Furthermore large correlation of observed movement qualities and patients’ self-reported Quality of Life indicators could be shown.

**Conclusion:** The modules were regarded feasible. Moreover, the outcomes showed initial sensitivity to change. They should therefore be tested in various movement orientated Mind-Body-Therapies.


Abstracts:

**Objectives:** A systematic review was conducted to assess the effect of vitamin E on the severity and duration of Cyclic Mastalgia compared to vitamin B6, fish oil, herbal medicines and placebo.

**Design:** A systematic review and meta-analysis of clinical trials.
**Methods:** A search was carried out in PubMed, Cochrane Library, Embase, Scopus and Google Scholar and Persian databases for articles published from 1980 to 2018. The data obtained were analyzed in RevMan and reported in forest plots. The Odds Ratio (OR) was used to find the effect for the dichotomous data and the Standardized Mean Difference (SMD) for the continuous data. The heterogeneity of the studies was assessed using I² and the Random Effects Model was used instead of the Fixed Effects Model if I²>25%.

**Results:** A total of 1051 titles and abstracts were extracted. Fourteen articles ultimately remained, and 11 of them were entered into the meta-analysis. The meta-analysis showed significant differences between vitamin E and placebo in the severity (SMD=−0.51; 95% CI=−0.21 to −0.82) and duration (MD=−1.47; 95% CI=−0.91 to −2.57) of cyclic mastalgia, although herbal medicines had a greater effect on the severity of mastalgia than vitamin E (SMD =0.51, 95% CI =0.06 to 0.96).

**Conclusion:** Although herbal medicines are more effective than vitamin E, vitamin E reduces both the severity and duration of the disorder compared to placebos, which only reduce its severity, and can therefore be considered a treatment with minimum side-effects. Due to the high heterogeneity of the studies, the researchers recommend further research on the subject using a standard tool based on the CONSORT statement.


**Abstract:**

**Introduction:** Yin-Yang is a major clinical theory of East-Asian traditional medicine for evaluating biopsychological and pathophysiological features. The purpose of current study was to evaluate the Yin-Yang personality of pediatric outpatients using Sasang Personality Questionnaire (SPQ) which has been used for both adolescents and adults.

**Methods:** A total of 249 pediatric outpatients completed the SPQ, and respondents were divided into two groups - toddlers and preschoolers (age 1–6, n = 153) and elementary students (age 7–12, n = 96). Gender differences in the SPQ were examined using the Chi-squared test and t-test, and chronological changes of Yin-Yang personality were illustrated with Pearson’s correlation and boxplots.

**Results:** The psychometric features of the SPQ in pediatric outpatients were in accordance with those previously reported in community children. The correlation between age and SPQ was not significant (r =0.049, n.s.) in elementary students, which was consistent with previous studies; however, a significant negative correlation (r =-0.351, p < 0.01) was found in preschoolers.
Data showed that the Yang personality is strongest at age one and decreases throughout preschool ages.

Conclusions: The chronological characteristics of Yin-Yang personality of preschoolers with SPQ might be useful for understanding East-Asian traditional pediatric theories from a biopsychological perspective. The clinical implications of the current results in person-centered prevention and health promotion were discussed.


Abstract:

Objectives: Population-based information on the costs of complementary medicine for treatment-related side effects in patients with breast cancer is scarce. We aimed to investigate the prevalence and expenditure on complementary medicine in patients with breast cancer who experienced treatment-related side effects.

Design and setting: Two datasets were analyzed: 1) a 2017 survey on direct and indirect costs for treatment-related side effects, which was completed by 100 patients with stage 0-IV breast cancer, and 2) a Korean representative cross-sectional survey (Patient Survey 2014) that examined the prevalence of integrative medicine in 41 patients with breast cancer.

Main outcome measures: The direct and indirect costs for treatment-related side effects.

Results: In the first dataset, the mean total direct medical cost for complementary medicine was US$1,584 and the mean indirect cost was US$6,988 per patient per year. Some patients (6%) visited non-medical institutions to utilize complementary medicine and additionally spent US$460 per patient per year. Approximately one-third of participants reported a substantial-to-heavy financial burden for using complementary medicine. However, only 17% of patients got information about complementary medicine through their physician. In the second dataset, 49% of patients with breast cancer who were discharged from Korean Medicine hospitals in Patient Survey 2014 data indicated that integrative medicine had been used.

Conclusions: Despite some complementary medicine could be reimbursed by National Health Insurance in Korea, a considerable number of patients reported an economic burden associated with their use of complementary medicine. Strategies for guiding patients to receive evidence-based and cost-effective complementary medicine are needed.

Harnett Joanna E., Ung Carolina Oi Lam, Hu Hao, Sultani Mustafa et al. Advancing the pharmacist’s role in promoting the appropriate and safe

**Abstract:**

**Background:** Natural products (NPs) are widely purchased as dietary supplements (DS) in pharmacy outlets. U.S. pharmacists report multiple barriers in adopting a professional role that ensures the appropriate and safe use of DS.

**Objective:** To elicit pharmacist and key stakeholder perceptions about the actions needed to enable pharmacists to fulfill a professional role related to DS use.

**Methods:** An interview guide was developed based on the existing literature. A grounded theory approach involving in-depth, semi-structured key informant audio-recorded phone interviews. Audio recordings were transcribed verbatim, and thematic analysis using open coding, grouping, and categorizing into emergent themes was conducted.

**Results:** 22 interviews were conducted with 12 practicing pharmacists and 10 organizational representatives. In general, pharmacists proposed they could develop and promote themselves in this area, and all participants offered opinions about the actions they believed would facilitate the development of a more structured service and formalized role for pharmacists providing care related to DS use. Four key areas were identified (1) Education and training; (2) Strategies for ensuring high standards related to DS safety and quality assurance (3) Workplace resources (4) DS Research.

**Conclusions:** Despite the challenges facing pharmacy related to DS use, pharmacists and key stakeholders hold constructive and practical ideas about how to transform the current DS landscape into an opportunity that develops pharmacist’s professional role and facilitates the appropriate and safe use of DS by Americans.


**Abstract:**
**Objective:** Sauna-bathing is an ancient tradition that is gaining popularity across the world as a wellness tool. There is a growing body of medical evidence supporting the role of saunas, or whole-body thermotherapy, as a form of treatment for a range of health issues. However, the demographics, motivations and experiences of current sauna bathers have not yet been explored on a global scale. This study is designed to explore these themes.

**Design:** An online 71-item questionnaire compiling information on the individual characteristics, sauna-related habits and perceived health and wellness experiences of regular sauna bathers was conducted from October 2016 to October 2017. The validated ‘SF-12’ quality of life scoring tool was incorporated into the questionnaire to measure physical and mental indicators of well-being.

**Results:** Of 572 logins recorded, 482 valid responses were generated. Both men (51.3%) and women (48.7%) were represented, and respondents were predominantly well-educated (81.8%), non-smoking (90.6%), regularly-exercising (78.8%) individuals of normal-to-overweight status (87.1%) who sauna-bathed approximately 1–2 times per week. The key reasons indicated by respondents for sauna-bathing included relaxation/stress reduction, pain relief and socializing. Nearly a third of respondents reported medical conditions and of this subset, those with back/musculoskeletal pain and mental issues cited the greatest improvements in their conditions with sauna-bathing. Of all respondents, 83.5% reported sleep benefits after sauna use. Analysis of well-being scores after stratifying respondents into three groups by sauna-bathing frequency (group I: <5 times per month; group II: 5–15 times per month; group III: >15 times per month) revealed group II respondents had slightly higher mental well-being scores (Kruskal–Wallis testing: $H = 6.603 > \chi^2$ of 5.991, $p = 0.0368$, df = 2 with post hoc analysis using Mann–Whitney $U$ test: $p = 0.016$) as compared to respondents who were sauna-bathing less frequently (group I). No respective differences were detected between the physical well-being scores of any of the three groups. Adverse reactions to sauna-bathing were recorded as mostly minor (93.1%), including primarily symptoms of dizziness, dehydration and headache. However, there were two reports (0.3%) of chest pain and eye irritation requiring hospitalization.

**Conclusions:** This cross-sectional study documents that sauna-bathing participants, particularly those from Finland, Australia and the United States, are motivated to use saunas predominantly for relaxation, reporting health benefits especially around mental well-being and sleep, with relatively few adverse effects. While these results reinforce some of the known health benefits of sauna bathing, they indicate that further research and better dissemination of existing evidence is needed to fully develop the sauna’s potential as a therapeutic intervention.

Irmak Zöhre, Tanrıverdi Özgür, Ödemiş Hilal, Uysal Derya Demir et al. Use of complementary and alternative medicine and quality of life of

**Abstract:**

**Objectives:** This study aims to evaluate the frequency of use of CAM therapies among cancer patients, the types of CAM therapies they used, the demographic and clinical factors affecting their tendency to use CAM therapies, and the difference between quality of life of CAM user and non-user patients.

**Design:** This cross-sectional study was carried out between March and June 2016 in an education and research hospital located in Mugla, Turkey. A CAM use questionnaire, the European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire (EORTC QLQ-C30 version 3.0) and the Nightingale Symptom Assessment Scale (N-SAS) were administered to 211 patients.

**Results:** Among all the participating patients, 46.4% were CAM users. The most commonly used CAM therapy was herbal products. The rate of CAM use was higher among the patients with a low education level (P = 0.004). No statistically significant difference was found between the quality-of-life scores of the CAM user and non-user patients.

**Conclusion:** Almost half of the cancer patients used CAM therapy, with the most commonly used CAM therapy being herbal products. Doctors/nurses should assess patients in terms of the CAM therapies they use to determine their possible side effects and drug interactions. Further research should be performed to determine the relationship between CAM therapy and quality of life.


**Abstract:**

Flu is an acute respiratory illness caused by influenza virus. The data shows that the incidence of seasonal influenza is on the rise. Much of the illness caused by influenza treated by homoeopathy i.e. the science which is concerned primarily with the unique way in which each individual manifests their symptoms and we have to determine the most prominent or characteristic symptom. And to finding out the simillimum repertory is an important tool for a homoeopathic practitioner and which also helps in elimination of the non indicated drugs. Rubrics with single medicine are verified clinically then only included in repertory,i.e if a rubric has single medicine in front of it them it definitely has curative action in homoeopathy In this article such a case of flu is presented where indicated medicine, which was a single remedy rubric was prescribed after confirming it by cross repertorization. Medicine showed positive outcome in this case.
Abstract:

Introduction: Little is known about integration of Complementary and Alternative Medicine (CAM) in the Dutch healthcare system. The aim of the present study was to investigate how Integrative Medicine (IM) is practiced and how CAM is integrated with conventional medicine in curative and long-term healthcare centres in the Netherlands.

Methods: A mixed methodology was applied, including a systematic internet search, an online survey and focus groups among healthcare professionals.

Results: Most hospitals (92%) offered some form of CAM to treat anxiety (72%), restlessness (68%), pain (65%), sleeping problems (50%), stress (48%) and fatigue (36%). Mostly offered modalities were relaxation exercises (88%), art therapy (44%) and mindfulness (42%). Similar percentages of CAM use were found in other healthcare centres. Most CAM modalities were implemented without organizational vision, guidelines or protocols. Only 5% of implemented CAM was labelled as IM. Focus groups with health care professionals revealed the need to increase knowledge and to develop a vision for integration of CAM with conventional medicine, as well as to support effectiveness research in this area.

Conclusions: This study is the first in the Netherlands to quantitatively map the extent of CAM integration in conventional health care. The number of CAM interventions offered at conventional health care settings was surprisingly high. However, integration was fragmented. Guidelines, education and research programs are needed to further integration of CAM, preferably organised in a Dutch Consortium for IM.


Abstract:

Homeopathic rescue of a mentally tormented lady falling prey to black magic.


Kancharla Trusha. I am 28, but still wet the bed! *National Journal of Homoeopathy* 2019; 21 (6) 237th; 40-42p

**Abstract:**

From this case I learnt two rubrics, Rage has to be chained, delusion poor.


**Abstract:**

**Objectives:** The purpose of this research was to investigate the effect of *Urtica dioica* in comparison with placebo, acupuncture and combined therapy on hot flashes and quality of life in postmenopausal women.

**Methods:** In a double-blinded randomized controlled trial, patients were treated for 7 weeks then followed up 4 weeks. Seventy-two postmenopausal women who reported at least 20 hot flashes attacks per week were randomly allocated into one of the 4 groups of *Urtica dioica* 450 mg/day and acupuncture 11 sessions (A), acupuncture and placebo (B), sham acupuncture and *Urtica dioica* (C), and sham acupuncture and placebo (D). The primary outcomes were the change in hot flashes score from baseline to the end of treatment and follow up; and the change in the quality of life (MENQOL) from baseline to the end of treatment. Secondary outcomes included changes in FSH, LH, and ESTRADIOL levels from baseline to the end of treatment. The trial was conducted from October 2017 to July 2018 in Acupuncture clinic of a teaching hospital in Iran.

**Results:** A total of 72 women 45–60 years old were enrolled, and 68 were included in the analyses. The median (IQR) hot flashes score decreased in the A group by 20.2 (31.7) and 21.1 (25.1), B group by 19 (18) and 17.3 (27), C group by 14.6 (25.4) and 20.8 (13), and D group by 1.6 (11.6) and 1 (13.3) at the end of treatment and follow up (P < 0.0001, P < 0.0001); no significant difference between A, B and C groups. The mean (SD) of MENQOL score decreased in the A group by 42.6 (21.1), B group by 40.7 (29.8), C group by 37.8 (26.8) and D group by 9.8 (14.3) at the end of treatment (P = 0.001); no significant difference between A, B and C groups.

**Conclusions:** *Urtica dioica* can decrease menopausal hot flashes and increase the quality of life of postmenopausal women better than placebo-sham control but same as acupuncture. The combination of *Urtica dioica* and acupuncture did not add to the effects of those therapies.

Abstract:

**Objective:** Music can be used as an alternative method to decrease anxiety in awake patients during surgical procedures. The aim of this study was to test the hypothesis that listening to music during carotid endarterectomy (CEA) under regional anesthesia decreases the patient’s anxiety and pain.

**Design:** A multicenter, prospective, randomized controlled trial.

**Setting:** Patients undergoing carotid endarterectomy under cervical plexus block.

**Interventions:** Patients scheduled for carotid endarterectomy under cervical plexus block were randomized into two groups: Music Group and Control Group.

**Main Outcome Measures:** The primary endpoint of this study was the difference in intraoperative anxiety in patients with or without music during CEA under regional anesthesia, and the secondary endpoints were intraoperative and postoperative pain, use of additional local anesthetics, use of intravenous analgesics, patient and surgeon satisfaction and complications. Anxiety was assessed using State Trait Anxiety Inventory (STAI) and numeric rating scale (NRS). Visual analog scale (VAS) was used for pain assessment.

**Results:** The postoperative STAI scores were similar in both groups (p = 0.839). The NRS scores measured immediately after the end of the surgery were statistically higher in Music Group (p = 0.001). The intraoperative anxiety statistically increased in Music Group, when the scores of the intraoperative responses to the questions of “are you relaxed?” and "are you calm?” were compared. (p = 0.0001 and p = 0.0001, respectively). There were no statistical differences in terms of the amount of intraoperative and postoperative analgesic used (p = 0.801, p = 0.773, respectively). The intraoperative VAS scores, postoperative VAS scores, patient and surgeon satisfaction scores were similar in both groups (p = 0.586, p = 0.185, p = 0.302 and p = 0.599, respectively). Systolic, diastolic and mean arterial blood pressure and heart rate were no different between Music Group and Control Group at any of all time points during the intraoperative period. Surgical side and contralateral side cerebral rSO2 values are similar in both groups (p = 0.438, p = 0.397, respectively).

**Conclusions:** Music use in CEA under regional anesthesia increased intraoperative patient anxiety, and had no effect on intraoperative and postoperative pain or patient satisfaction.


Abstract:

Objectives: In the present study, the reaction of blood pressure and heart rate are examined during and after a single acute sauna application.

Design: In 19 healthy adult volunteers (7 women, aged 46.4±10.2 years, BMI 24.4±2 kg/m²), blood pressure (BP) and heart rate (HR) were measured during a 25-minute sauna session (93°C, 13 % humidity) and during a subsequent 30-minute rest period. The parameters obtained were compared with the BP and HR responses during submaximal dynamic exercise testing.

Results: The heat exposure resulted in a significant (p<0.01) and progressive increase in systolic and diastolic BP. After the sauna bath, BP decreased and showed significantly (p<0.001) lower values compared to baseline. HR also increased continuously during heat application (p<0.001), resulting in a significant increase (p<0.001) in systolic BP x HR as a measure of myocardial oxygen consumption. After the end of the sauna session, both the BP and the HR decreased steadily (p<0.001). When comparing BP and HR during the sauna session with the reaction during a dynamic exercise test, sauna bathing was equivalent to an exercise load of about 60-100 watts.

Conclusions: Contrary to popular belief, acute sauna use does not lead to a reduction, but to an increase in BP and HR with a consequent increase in myocardial oxygen consumption. The cardiac load during the sauna use corresponds to a moderate physical load of 60-100 watts.

Khaleque Abdul. Patience is bitter but its fruit is sweet. National Journal of Homoeopathy 2019: 21 (6) 237th; 48-54p

Abstract:

Hahnemann’s three Chronic Miasms- Psora, Sycosis and Sycosis and Syphilis are operative behind all chronic diseases. The psoric itches; the sycotic infiltrates (a causes of excess in growth) and corrodes with discharges and the syphilitic ulcerates and deforms and degenerates the bony structure. In treating chronic diseases it is essential to consider these Miasms. It is necessary to know whether the symptoms presented are of sycotic, syphilitic or psoric origin, for the totality must be about the symptoms of the active miasm. In selecting the remedy we should arrange the symptoms giving preference to those last appearing, for they are the symptoms of the active miasm and in the process of cure they are to be removed first. One should know that an itching irritability is psoric, a fungous growth or uric acid
diathesis is sycotic while a degenerative growth is both sycotic and syphilitic. Thus one has to identify each of the signs and symptoms of the patient under the active and underlying misaims. In cases of grave pathology the first prescription should cover along with the presenting symptoms, the organ, the site or locality of present affection in the patient.

**Khurana Anil. Update on evidence based research by ccrh. Medicina Futura Homoeopathica 2019; 7(6): 9-15p.**


**Abstract:**

**Objectives:** To evaluate the antihypertensive efficacy and safety of a standardized Vaccinium arctostaphylos (V. arctostaphylos) berry hydro-alcoholic extract in the overweight/obese hypertensive patients.

**Design:** Randomized placebo-controlled trial.

**Setting:** Baqiyatallah hospital (Tehran, Iran).

**Interventions:** The antihypertensive efficacy and safety of 3-month intake of 400 mg extract capsule three times daily alongside standardized antihypertensive regimen in the treatment of 50 patients was compared with the placebo (n = 50).

**Main outcome measures:** SBP (systolic blood pressure), DBP (diastolic blood pressure), body mass index, waist circumference, CBC (complete blood count), blood levels of AST (aspartate aminotransferase), ALT (alanine aminotransferase), ALP (alkaline phosphatase), BUN (blood urea nitrogen) and creatinine.

**Results:** SBP decreased from 152.1 ± 7.7 to 140.5 ± 10.7 in the V. arctostaphylos group and from 152.9 ± 8.1 to 150.8 ± 9.3 in the placebo group (P < 0.001). DBP decreased from 90.3 ± 8 to 82.1 ± 8.8 in the V. arctostaphylos group and from 89.6 ± 7.8 to 87.6 ± 7.9 in the placebo group (P < 0.001).

The extract capsule had no significant effect on the other parameters (P > 0.05). Moreover, no drug side effect and adverse interaction with other antihypertensive drugs was observed in the patients.

**Conclusions:** V. arctostaphylos berry extract improves blood pressure control and has safety and tolerability in the overweight/obese hypertensive patients taking standard antihypertensive drugs.

Abstract:

Objectives: To investigate the inhibitory effects of an herbal formulation of Cheongsangbangpoong-tang (CBT) on inflammatory acne lesions as the control of the ‘Heat’ pattern.

Design: A single center study. Randomized, placebo-controlled, parallel group, double-blind trial

Setting: Fifty-six subjects, who had more than 10 acne inflammatory lesions each, were randomly allocated into the CBT or placebo groups and took 5 g CBT extract (CBT group) or 5 g placebo extract (control group), respectively, three times a day for 8 weeks. Pattern identification change of the inflammatory and non-inflammatory acne lesions, temperature of the facial points, serum cortisol level, serum dehydroepiandrosterone-sulfate level, number rating scale, investigator global assessment (IGA), and severity score on the Korean acne grading system were measured.

Main outcome measure: mean change of the inflammatory acne lesions.

Results: After CBT/placebo administration, the percentage count of inflammatory lesions in subjects was significantly reduced in the CBT group when compared with the control group. The other outcomes showed no significant difference between the two groups. On pattern identification, subjects with the Wind-Heat pattern (風熱型, WHP) and Disharmony of the thoroughfare and conception vessels pattern (衝任不調型, DTCVP) tended show better effect than those with other patterns.

Conclusions: CBT is a potential therapeutic agent for the treatment of acne vulgaris, linked to inhibition of inflammatory lesions and facial heat.


Abstract:

Background: Hyperemesis gravidarum (HG) is generally characterized by intractable nausea and vomiting which interferes with daily life. As the cause of HG has not yet been clearly identified, conventional medicine therapies
address only the symptoms. Conventional treatment is also effective for a comparatively short time and may have unfavorable side effects. Given that the condition affects more than 1% of pregnant women, there is a significant need for effective long-lasting treatments with limited side effects.

**Case reports:** This paper is based on three case reports of pregnant women suffering from HG. They received inpatient treatment based exclusively on anthroposophic medical approaches at the Paracelsus Hospital Richterswil, Switzerland. Treatments were selected individually based on the specific patient profiles and included infusion therapy with Nux vomica, Solum uliginosum compositum and Bryophyllum pinnatum as well as art therapy (wet-on-wet painting), eurythmy therapy and rhythmical massage therapy. Anthroposophic complex therapies induced an improvement in symptoms of nausea and vomiting within one week in all three cases.

**Conclusion:** Anthroposophic complex therapy is a valuable option in the treatment of HG. Well-tolerated and long-lasting, it represents a holistic and causal approach that does not only address symptoms.


**Kumbhejkar Shrinivas C, Suman CH K. Health care sector -present scenario from the view point of medical practitioners.** *Homoeopathy The Friend of Health 2019; 7(6): 10-12p.*


**Abstract:**

**Introduction:** Associations between psychological stress and the development of cardiovascular events and stroke have been established. Meditation is recognized as a method to reduce the stress. The aim of this study was to investigate the anthropometry, serum glucose and serum cholesterol status in monks practicing Samatha and Vipassana meditation living in forest hermitages.

**Methods:** This cross-sectional study compared 115 meditating Buddhist monks (71 meditating >6 months, 45 meditating <6 months) to 137 non-meditating subjects (36 non-meditating monks and 101 laymen). Body mass index, systolic and diastolic blood pressure, fasting blood sugar and lipid profile were measured. Meditation duration and dietary assessment was evaluated using an investigator administered questionnaire.

**Results:** From parameters tested, the HDL cholesterol level was higher (53.8 ± 5.3 mg/dL) (P<0.001) while total cholesterol: HDL ratio was (3.57 ± 0.52) significantly (P<0.0036) lower in monks meditating for >6 months compared with naïve (<6 months) meditating monks (4.1 ± 0.53), non-
meditating monks (4.6 ± 0.93) and non-meditating laymen (5.5 ± 1.6). Systolic and diastolic blood pressures, pulse rate, serum glucose and non-HDL cholesterol did not vary significantly among these groups and were within normal limits.

**Conclusion**

Meditating monks had a higher HDL cholesterol, lowest total cholesterol: HDL ratio and the other parameters tested had mean levels closer to the lower limit of the normal range, indicating a possible protective effect of meditation on cardiovascular diseases and stroke. These results may be related to the duration of practicing Samatha and Vipassana meditation but require confirmation using appropriate clinical trial methodology.

**Kunapareddy Siva Shankar.** Queues at spinal surgeons clinics are lengthening. *Medicina Futura Homoeopathica* 2019; 7(6): 5p.


**Abstract:**

**Background:** This study aimed to explore the effectiveness of acupuncture combined with tuina therapy in patients with migraine.

**Methods:** A prospective, randomized controlled assessor-blind clinical trial was performed between January 2017 and May 2018, and 135 patients were assigned into acupuncture combined with tuina (A), acupuncture (B), and control (flunarizine hydrochloride) (C) groups, each with 45 patients. Treatments were performed for 12 weeks and a 4-week follow-up. Frequency of attacks, severity of pain, duration of migraine, associated symptoms, patient-reported outcome (PRO) scores, and frequency of analgesic consumption were assessed.

**Results:** The total effective rate was 95.6, 88.9, and 75.6% for group A, B, and C, respectively, with a significant reduction in attack frequency, severity of pain, duration of migraine, and associated symptoms at post-treatment and follow-up compared to pre-treatment. The PRO scores and frequency of analgesic consumption were significantly improved (group A, \( p < 0.01 \); groups B and C, \( p < 0.05 \)). The differences in pre-/post-treatment and in pre-treatment/follow-up in groups A and B were significantly improved compared to group C (A vs. C, \( p < 0.01 \); B vs. C, A vs. B, \( p < 0.05 \)). No significant adverse events occurred.

**Conclusion:** Acupuncture combined with tuina could significantly increase the therapeutic effect of acupuncture in migraine treatment.

Abstract:

**Objectives:** This study aims to explore the treatment interventions complementary and integrative medicine (CIM) practitioners use in the management of an emerging health condition, increased intestinal permeability (IP), and the association these methods have on the observed time to resolve this condition.

**Design and setting:** A cross-sectional survey of Australian naturopaths, nutritionists, and Western herbal medicine practitioners was undertaken (n=227) through the Practitioner Research and Collaboration Initiative (PRACI) network.

**Outcome measures:** Frequencies and percentages of the treatment methods, including chi-square analysis to examine the associations between treatment methods and observed time to resolve IP.

**Results:** Thirty-six CIM practitioners responded to the survey (response rate 15.9%). CIM practitioners were found to use a multimodal approach in the management of IP with 92.6% of respondents using three or more categories of treatment interventions (nutritional, herbal, dietary, and lifestyle) with a mean total of $43.0 \pm 24.89$ single treatment interventions frequently prescribed. The main treatments prescribed in the management of IP were zinc (85.2%), probiotics: multistrain (77.8%), vitamin D (75.0%), glutamine (73.1%), *Curcuma longa* (73.1%), and *Saccharomyces boulardii* (70.4%). CIM practitioners also advocate patients with IP to reduce alcohol (96.3%), gluten (85.2%), and dairy (75.0%) consumption. Evaluation of antibiotics (75.0%) and nonsteroidal anti-inflammatory drugs (73.1%) prescriptions were frequently advised by CIM practitioners. A longer observed time to resolve IP was seen in CIM practitioners who did not reduce intense exercise in the management of IP ($p = 0.02$).

**Conclusions:** This study represents the first survey of the treatments prescribed by CIM practitioners for IP and suggests that CIM practitioners use numerous integrative treatment methods for the management of IP. The treatment interventions frequently prescribed by CIM practitioners align with preclinical research, suggesting that CIM practitioners prescribe in accordance with the published literature. The findings of this study contribute to the implementation of clinical research in the management of IP, which considers multiple concurrent treatments.


Abstract:
**Introduction:** The World Health Organization has reported that approximately 35% of cancer-related deaths are attributed to modifiable risk factors. Among the most important risk factors amenable to modification are obesity and lack of physical activity. The purpose of this article is to review the current evidence of the benefits of physical activity in various types of cancer.

**Methods:** A PubMed search for the key words “physical activity and cancer” as well as “exercise and cancer” was used to identify all indexed publications on this topic for potential utilization in this review. One MET was defined as the amount of oxygen consumed while a person is sitting quietly and is about 3.5 mL O2/kg body weight/min. MET represents the ratio of the working metabolic rate to the resting metabolic rate.

**Results:** Routine physical activity was found to be associated with a reduced incidence of several of the most common malignancies, including colon, breast, lung, and endometrial cancer as well as many others. Physical activity also appears to reduce all-cause mortality and cancer-related mortality among patients with breast and colon cancer, and may improve the functional status and quality of life for these patients during cancer therapy.

**Conclusions:** The benefits of physical activity in the prevention and progression of cancer patients are multiple. However, the strength of the available evidence is limited by the observational nature of most studies. Given the probable improvement in prevention, mortality, and quality of life with structured physical activity in different malignancies, it is important that healthcare providers discuss physical activity programs with their cancer patients. Larger randomized trials are recommended.

**Abstract:**

Bee products including propolis, bee wax, pollen and royal jelly (RJ) have been used as medicine from ancient times. A vast number of in-vivo and in-vitro studies as well as clinical trials have been conducted to investigate potential health related properties of RJ. A growing number of clinical trials have been performed to assess effects of RJ ingestion on different metabolic markers including glycemia, with diverse results. In the current meta analysis, we aimed to evaluate effects of RJ ingestion on glycemic markers compared with placebo and set directions for future research. Electronic databases including Scopus, Pubmed, Scholar, Cochrane, Proquest, SID and Magiran were searched and 5 eligible studies were included in the quantitative analysis. Review Manager Software was used for statistical analysis and random effects model was used for pooling data. A total of 205 participants for FPG and 130 participants for HbA1c were included. The overall analysis revealed that RJ consumption reduced FPG by 0.95 mg/dl (95% CI: −5.83 to 3.87; p = 0.69; I2 = 0%; Tau² = 0.00) and HbA1c by 0.32 (95% CI: −0.87 to 0.23; p = 0.25;
I² = 69 %; Tau² = 0.16) which were not statistically significant. Funnel plot demonstrated no publication bias. In conclusion, RJ supplementation did not beneficially affect markers of glycemia. However, due to methodology issues and potential confounders like diet as well as diverse populations, we recommend future studies well designed and well controlled for major confounders so we can update these data to more precise results and more accurate conclusion.


Abstract:

Objective: Diet plays a critical role in the management of non-alcoholic fatty liver disease (NAFLD). Studies on the NAFLD’s experimental models have reported that soy had positive effects on the improvement of metabolic parameters. However, there is a lack of clinical trials regarding the efficacy of whole soy foods. Therefore, this study was conducted to determine the effect of soy milk on some of the metabolic characteristics in patients with NAFLD.

Methods: Sixty-six patients diagnosed with NAFLD were included in this randomized, parallel, controlled trial and were randomly assigned to either the soy milk or control group. Both groups received a 500-deficit calorie diet plan. Also, patients in the soy milk group consumed 240 ml/day soy milk for 8 weeks. Fasting blood sugar (FBS), serum insulin, HOMA-IR, HOMA-β%, and QUICKI as well as serum malondialdehyde (MDA), plasma fibrinogen, and blood pressure (BP) were measured at the beginning and end of the study.

Results: After 8-weeks of intervention, soy milk group had a greater significant reduction in serum insulin(-3.44 ± 5.02 vs. -1.09 ± 3.77 μIU/ml, P = 0.04), HOMA-IR (-0.45±0.64 vs -0.14 ± 0.47, P = 0.03), systolic (-3.81±4.15 vs -1.48±2.93 mmHg, P = 0.01) and diastolic (-2.39±2.80 vs. -0.94±2.76 mmHg, P = 0.04) BP, and also, a significant increase in QUICKI (0.02± 0.032 vs. 0.008±0.018, P = 0.04) compared to the control group. While, changes in the FBS, HOMA-β%, fibrinogen, and MDA were not significantly different between the study groups.

Conclusion: A low-calorie diet containing soy milk had beneficial effects on serum insulin, HOMA-IR, QUICKI, and BP in patients with NAFLD.


Medeiros Natasha Teixeira, Catrib Ana Maria Fontenelle, Melo Naiana Anchieta Mendes, Holanda Gabriela Pessoa Marinho et al. Academic

**Abstract:**

**Objectives:** To assess the association of academic education in health professions programs with the knowledge and use of Complementary and Alternative Medicine (CAM) by university students and to determine whether CAM can promote a healthy university environment.

**Methods:** A cross-sectional study was carried out with 512 university students enrolled in health professions programs in the city of Fortaleza, Ceará, Brazil, from April to November 2017. The Assessment Tool for Health Promotion at the University was used to collect sociodemographic, academic and CAM data. Bivariate and multivariate analyses were performed considering the outcomes “knowledge of CAM” and “CAM in the promotion of a healthy university environment” using SPSS Statistic version 20.0.

**Results:** Data from 512 participants were analyzed. Women (n = 357; 69.7%), young students (n = 393; 76.8%) and unemployed students (n = 429; 83.8%) predominated. Knowledge of CAM was associated with health profession program (OR = 0.934; p = 0.047), paternal education (OR = 0.641; p = 0.024), employment (OR = 0.542; p = 0.028) and participation in extracurricular activities (OR = 1.275; p = 0.007). There was a proportional difference between knowledge and use of CAM ranging from 2:1 to 11:1 among the 21 modalities. University students believed that CAM could promote a healthy university environment (p = 0.000), which was influenced by gender (OR = 2.089; p = 0.004) and knowledge of CAM (OR = 16.601; p = 0.000).

**Conclusions:** University students’ knowledge of CAM was influenced by the health profession program, paternal education, employment and participation in extracurricular activities. The percentage of use of CAM modalities was lower than the percentage of knowledge. University students’ belief that CAM could foster a healthy university environment is influenced by gender and knowledge of CAM.


Abstract:

Introduction: Both resistance and stretch-shortening cycle exercise have positive effects on physical abilities and health related factors. In the present experiment we tested the hypothesis that an 8-week-long combined strength and stretch-shortening cycle exercise training is superior to strength training alone in the development of walking and running economy in healthy untrained women.

Methods: Twenty untrained female college students (age = 21.5 ± 2.1 years, body mass index = 22.3 ± 2.9) were divided into two experimental groups. Both groups performed own-body resistance exercises three times per week but one group performed additional stretch-shortening cycle exercises. Countermovement jump force as well as maximal voluntary isometric torque and elastic energy storage and re-use in quadriceps muscle were measured. Running and walking economy was quantified by measuring maximal oxygen consumption during a treadmill test.

Results: Isometric torque improved uniformly in the two groups (p < 0.05), however countermovement jump force, elastic energy storage and re-use as well as running economy improved selectively after strength and additional stretch-shortening cycle exercise (p < 0.05). Walking economy was unaffected in either of the experimental groups.

Conclusion: This study suggests that improved elastic energy storage and re-use rather than maximum muscle contractility may account for the changes in countermovement jump force and running economy after additional stretch-shortening cycle exercise. The present data should be taken into consideration for understanding the favourable effects of stretch-shortening cycle exercise training in the young untrained population.


Abstract:

Objectives: As the popularity of complementary and alternative medicines (CAM) is increasing, it is important to understand the characteristics of people that make them to be attracted toward CAM and influence their attitudes. The purpose of the present study was to examine the associations between the socio-demographic characteristics of people as assessed by the a five-factor model and the attitudes toward CAM modalities among Turkish academicians.

Design: An online survey was completed by 227 academicians who were working in three leading universities of Turkey.
Main outcome measures: The academicians were queried anonymously on socio-demographics and which CAM modalities they utilized, by filling out the Ten-Item Personality Inventory (TIPI) and the Holistic Complementary and Alternative Health Questionnaire (HCAMQ).

Results: In regard to the intention of using a CAM modality in the academicians, 75.3% of the academicians specified an intention to use at least one form of CAM in their lives. Among all the academicians surveyed, 38.8% reported using at least one form of CAM in the previous year. The most widely used forms of CAM observed were herbal therapies and mind-body therapies (18.5%), touch-based therapies (15.4%), and multi-vitamin (4.8%). The ratio of CAM usage in the previous year was observed to be lower in the academicians working in the health-related professions. The present study also identified that the academicians with openness personality-type exhibited greater positive attitudes toward CAM (p < 0.05).

Conclusions: The findings of the present study indicated that the academicians who are open to experience, as assessed by the five-factor model of personality, exhibited greater positive attitudes toward CAM. More than 60% of academicians agreed that CAM should be integrated into the curriculum, the remaining participants were unsure and disagreed. Therefore, the required feasibility studies to integrate CAM courses into the curriculum of Turkish medical and nursing schools are recommended as a priority.


Abstract:

Purpose: Childhood cancer survivors are at risk of treatment late-effects. Physical activity represents a necessary complementary therapy and modifiable risk-factor across all ages for many cardio-metabolic late-effects. This study assessed perceived physical activity in Australian and New Zealander childhood cancer survivors.

Methods: We recruited parents of survivors aged <16 years, and adult survivors of childhood cancer aged ≥16 years, ≥5 years since diagnosis, with age-matched controls for comparison. We compared perceived moderate-vigorous physical activity between survivors and controls, using regression to identify associations with physical activity.

Results: We recruited 914 participants (570 childhood cancer survivors and 344 age-matched controls). Parents of survivors perceived more moderate-vigorous physical activity than child controls (248 ± 218, 95% Confidence Interval [CI] = 218–280 vs 185 ± 214 min/week, 95% CI = 144–225, p = 0.036), with no perceived difference between adult survivors and controls (125 ± 152, 95% CI = 108–140 vs 160 ± 201 min/week, 95% CI = 132–187, p = 0.477).
Twenty-seven percent of child survivors (vs. 14.5% controls) and 30% of adult survivors (vs. 39.4% controls) met recommendations. Adult survivors who received radiotherapy (OR = 0.585, 95% CI = 0.343–0.995, p = 0.048) or not completed university (OR = 1.808, 95% CI = 1.071–3.053, p = 0.027) were less likely to meet recommendations.

**Conclusions:** Over two-thirds of Australian and New Zealander childhood cancer survivors across all ages are perceived to not meet physical activity recommendations. Adult survivors who had radiotherapy or did not complete university appeared at-risk for low physical activity.

**Practical implications:** Physical activity is important for everyone, but critical among childhood cancer survivors due to increased late cardio-metabolic risks. Monitoring survivors perceived but also objectively measured physical activity as complementary to routine care is warranted, to provide education and motivate survivors to take control of their health.


**Abstract:**

**Background:** The dichotic presentation of two auditory stimuli with a small frequency difference in each ear produces the perception of a third, fused auditory image called a binaural beat. Neural activity has been found to synchronize with these perceived beats. It is for this reason that binaural beats are often used in an attempt to induce certain psychological states that are associated with particular cortical rhythms. The aim of this proof-of-concept study was to explore the short-term effects of a binaural beat on tinnitus, to ascertain if further trials are justified.

**Method:** Twenty adults with constant tinnitus and symmetrical hearing underwent audiological assessment and psychophysical measures of tinnitus. Participants were presented with two auditory stimuli: ocean waves with and without alpha frequency (8 Hz) binaural beats. Arousal and tinnitus perception were measured prior to and following each sound stimuli using the Perceived Arousal Scale and tinnitus rating scales.

**Results:** Small improvements in tinnitus rating scores occurred with sound. Some individuals showed more improvement with the binaural beats than ocean waves alone.

**Conclusion:** The addition of binaural beats at 8 Hz to an ocean sound showed no significant group benefits above the ocean sound alone.

Abstract:

“We live and we die and anything else is just a delusion”… Truly said! We all are living in a virtual world today, fighting for virtual needs and struggling till the last breath for virtual satisfaction. All great writers, poets, painters and even scientist begin their work mere by working on “a delusion”! Once a unique idea strikes their mind, though unreal, it makes them think, re-think, over think and finally encourage them to work upon this virtual imagination (delusion) and undoubtedly leads them to success. However, medically speaking, delusion is merely a mental disorder. Hence, we are bound to focus more upon that. This article shall differentiate various types of delusions based on Present State Examination (PSE), along with examples in form of homoeopathic remedies.


Abstract:
The present write up is based upon cases presented at a state level seminar “Homoeopathic Approach in Rheumatological Disorders” organized by Aarogyam Aurangabad Doctor’s Association, Aurangabad.


Abstract:
Objective: This study aimed to assess the effects of chromotherapy on the cognitive ability of older adults.

Methods: This quasi-experimental pretest and posttest study was conducted among 135 older adults in Ilocos Sur, Philippines, between August and September 2015. The participants were divided into three groups: red, green, and white lights, with 45 people in each group. The cognitive ability of older adults was measured using an adapted Mini–Mental State Exam (MMSE).

Results: After the interventions, the red and green light experimental groups acquired a modest increase in cognitive ability scores against the comparison white light group ($p < 0.001$). However, the effects were not significantly different between the red and green lights postintervention ($p > 0.05$).

Conclusion: The chromotherapy is effective in improving the cognitive ability of older adults. Specifically, the red and green lights are better than the white light in increasing the cognitive ability of older adults.
Abstract:

Introduction: Memory problems are more common with ageing and are related to the development of Alzheimer’s disease. This study investigated whether the intake of lactobacillus fermented Saccharina japonica (FSJ) extract improved the cognitive function during working memory processing and whether biomarkers were associated with task performance.

Methods: Eligible participants were assigned to either a control group or an experimental group by computerized randomization. Participants were asked to take either 2 capsules, once a day for 4 weeks of lactobacillus FSJ for the experimental group or placebo control capsules for the control group. The cognitive function was determined using the Beck depression inventory (BDI), Korean Wechsler Adult Intelligence Scale (K-WAIS), operation-word span task and Raven’s test-based quantitative EEG test. Levels of amyloid-β, superoxide dismutase (SOD) in the serum using the ELISA were also measured.

Results: There was no significant difference between these two groups in all cognitive function tests using the independent sample t-test. However, the experimental group showed a significant difference in the correct answer percentage, concentration and left and right brain activity of space perception as assessed by the Raven test-based quantitative EEG test by a paired-sample t-test. Biochemical measurements showed, a slightly decreasing trend in amyloid-β, whereas SOD level was not significantly different between groups (P > 0.05).

Conclusion: These results suggest that FSJ may have the potential to improve cognitive function as evaluated by the Raven’s test via, regulation of SOD antioxidant system. Our findings provide preliminary evidence of the safety of FSJ and its potential to improve memory.


Abstract:

A closed, sac-like pocket of tissue that can form anywhere in the body. It may be filled with fluid, air, pus, or other material. Cysts can occur anywhere in the body and can vary in size.

**Abstract:**

Nocturnal enuresis (bed wetting beyond the age of 5 years) is fairly common in children. A very commonly seen problem in the clinic for which parents seek treatment & get concerned out of proportion. Homoeopathy is one of the best options for treatments of bed wetter as the children likes to eat sweet pills of homoeopathy.


**Abstract:**

**Background:** Irritable bowel syndrome with predominant constipation (IBS-C) is a common digestive disorder. The current therapy is inadequate and evidence regarding the effect of herbal therapies on the relief of affected individuals is insufficient. The aim of this study was to investigate the beneficial effects of flixweed and fig consumption on IBS-C symptoms.

**Methods:** 150 patients with IBS-C were enrolled in this randomized, controlled trial. All patients were randomly assigned to three groups and received an intervention for four months. The IBS severity score system and quality-of-life questionnaires were used for evaluating IBS-C symptoms. C-reactive protein levels, frequency of defecation and hard stool were also assessed.

**Results:** Consumption of flixweed or fig, compared to a control group, caused a significant improvement in IBS symptoms including frequency of pain, distention, frequency of defecation and hard stool. Also, the findings showed a significant increase in quality of life, as well as satisfaction with overall bowel habits. However, flixweed and fig intake had no significant effects on abdominal pain severity and C-reactive protein levels.

**Conclusions:** In conclusion, consumption of flixweed or fig for four months would be a useful therapy for alleviating IBS-C symptoms and can be a beneficial option for first-line treatment.

Abstract:

Objectives: The study aims to evaluate the therapeutic efficacy and safety of Chinese herbal medicine (Xiaoaiping) injections for chemotherapy-induced thrombocytopenia (CIT) in nonsmall cell lung cancer (NSCLC) and gastric cancer.

Design: A randomized, controlled, multicenter study from December 2013 to August 2015.

Settings/Location: All patients are from China.

Subjects: One hundred forty patients with either NSCLC or gastric cancer were enrolled in this trial.

Interventions: The intervention group (n = 70) was given Xiaoaiping injections (1 dose/day for 10 days) with chemotherapy, whereas the control group (n = 70) was given chemotherapy only. The follow up period was 11 days after the final injection.

Outcome measures: Platelet (PLT) count was tested at day 0, 7, 14, and 21 as the primary outcome for evaluation. Safety measurements, including red blood cells (RBC), hemoglobin (HBG), white blood cells (WBC), neutrophil (NE)#, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), creatine kinase (CK), creatinine (Cr), and blood urea nitrogen (BUN) were tested at day 0 and 21 as the secondary outcomes.

Results: (1) Two patients in the intervention group and four patients in the control group were lost upon follow-up. (2) PLT count: there was no significant difference in PLT count between the two groups from baseline (day 0), day 7, and day 14. At day 21, the intervention group indicated an upward trend of PLT count with a statistically significant difference than that of the control group (p < 0.05). (3) NSCLC: there was significant difference in PLT count on day 21 (p < 0.01). (4) Gastric cancer: there was no significant difference in PLT count between the two groups during this trial (p > 0.05). (5) There was no statistically significant difference between the intervention group and the control group with the safety figures (secondary outcomes) RBC, HGB, WBC, NE#, AST, ALT, LDH, CK, Cr, and BUN measured (p > 0.05). (6) Adverse events: one gastric cancer patient in the control group was diagnosed with gastrointestinal bleeding on day 3.

Conclusions: In conclusion, Xiaoaiping injections may provide a safe and effective option for CIT in patients with NSCLC.

Rivest-Gadbois Emmanuelle, Boudrias Marie-Hélène. What are the known effects of yoga on the brain in relation to motor performances, body

Abstract:

Objective: The current body of literature was reviewed to evaluate the effects of yoga on the brain in relation to motor performance, body awareness and pain.

Background: Yoga has been increasingly popular in the Western countries especially for its unique integration of the mind and body. Yoga has been studied more intensely in the last decade. Although it has been shown to improve cognitive functions, few studies have looked into the effects of yoga on improving motor performance, body awareness or pain and the possible underlying brain mechanisms associated with them.

Methods: A search of the current literature was made using keywords such as: “yoga brain motor”, “yoga brain pain”, “effects yoga brain” and “effects yoga brain motor performance”. The findings were then discussed in relation to motor performance, body awareness and pain and their reported mechanisms of action on the brain.

Results: A total of 61 articles were selected, out of which 29 were excluded because they did not meet our criteria. A total of thirty-two articles were included in this review, which we further subdivided by focus: motor performance (n = 10), body awareness (n = 14) and pain (n = 8).

Discussion: Our review shows that yoga has a positive effect on learning rate, speed and accuracy of a motor task by increasing attention and decreasing stress through a better control of sensorimotor rhythms. Yoga also seems to improve sensory awareness and interoception, regulate autonomic input, increase parasympathetic activity and promote self-regulation. Yoga was also shown to reduce the threat signal, increase pain tolerance, decrease pain unpleasantness and decrease the anxiety and distress associated with pain. Those changes are associated with the recruitment of specific brain areas such as the insula, the amygdala and the hippocampus.

Conclusion: Based on the studies reviewed in this report, we found that the practice of yoga seems to facilitate motor learning, to increase body awareness and to decrease pain. These are associated with a wide variety of changes in terms of brain activity and structure. Further studies are necessary to reveal its precise mechanism of action on the brain and to validate its wider application in clinical settings.

Abstract:

Objectives: There is an increasing body of literature documenting the efficacy of micronutrients (vitamins and minerals) interventions for the treatment of psychiatric problems in the short term; however, long-term safety is largely unexplored. The goal of this observational study was to investigate the safety of two commercially available broad-spectrum micronutrient formulas (EMPowerplus and Daily Essential Nutrients) given at doses above the Recommended Dietary Allowances for the long-term treatment of individuals with psychiatric symptoms.

Design: Participants on long-term treatment with micronutrients (medication-free) for psychiatric problems (attention-deficit hyperactivity disorder [ADHD, n = 21], anxiety/depression [n = 13]) were identified from ongoing research studies and the community through purchasing records. Seventeen children and 17 adults had blood tests to assess their full blood count, coagulation profile, liver and kidney function, fasting glucose, iron studies, key nutrients, and prolactin. Questionnaires assessed psychological/psychiatric functioning. Seventeen of the participants had completed the same measures pretreatment.

Results: The average length of consuming micronutrients was 2.66 years (standard deviation = 2.86). Excluding B12 (which was elevated for almost all participants), 94.6% of all blood test results were within the test reference ranges. One participant was diagnosed with hemochromatosis based on iron studies. No other clinically relevant adverse changes in blood results were identified pre- and post-treatment. No clinically significant adverse effects were reported. Post-treatment psychometrics identified that 85% of the participants were in nonclinical ranges for measures of ADHD, depression, anxiety, and stress.

Conclusions: We report preliminary evidence for the safety of long-term commercially available micronutrients, although questions remain. Overall, the substantial psychiatric benefits observed appear to outweigh the minimal observed risks in these participants. Screening for potential medical problems is recommended before initiating treatment. Long-term pharmacovigilance monitoring is required to ascertain any rare but significant adverse events.


Abstract:

Traumatically encoded memories can last a lifetime. These memories, either by purposeful or inadvertent re-activation, cause the release of stress hormones and generate a persistent and inescapable allostatic load on the body, brain and mind. This leads to a maladaptive response, as the ability to return to pre-event homeostasis is no longer possible. The consequence of this response is that it increases risk for further traumatization and other
disorders. Remarkably, recent research has shown that these memories become labile and subject to disruption upon recall. In this paper we outline conditions needed for an event to be encoded as a trauma and describe a method that abrogates the release stress hormones when cued by these memories of the event. Critical to this process is the AMPA receptor (so named for its specific agonist, AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid, a compound that acts as glutamate, its natural substrate). It is hypothesized that traumatic encoding requires increasing the number and permanence of AMPA receptors on the lateral nucleus of the amygdala by a process called synaptic potentiation. Depotentiation, that is removal of these AMPA receptors, is required for de-encoding. We speculate that the generation of oscillatory intracellular calcium waves is necessary for this to occur. Electromagnetic fields, acting as electroceuticals, interact with voltage-gated calcium channels on depolarized post-synaptic membranes to produce these intracellular calcium oscillations of varying frequency. These oscillatory calcium waves are decoded by intracellular calmodulin which, depending on the frequency, either act to potentiate or depotentiate AMPA receptors. This article describes the theory and practical application of a psychosensory approach called Event Havening that generates an electromagnetic field to synaptically depotentiate these encoded AMPA receptors and eliminate the effects of traumatic encoding.


**Abstract:**

The suppression of appetite with herbal medicines has become very popular in recent years. We conducted this systematic review to evaluate the recent scientific evidence regarding herbal medicines that are used to suppress appetite. We retrieved clinical trials from PubMed, Cochrane Central Register of Controlled Trials, Web of Science, Scientific Information Database, and IranMedex from January 1, 2013 to April 24, 2018. English and Persian language randomized clinical trials that used herbal medicines to suppress appetite in healthy or obese or overweight individuals were included. Risk of bias was assessed using Cochrane methodology. Out of 591 articles, 22 trials with 973 participants were included. One study on the Meratrim formulation which contained the Sphaeranthus indicus flower heads extract and Garcinia mangostana fruit, revealed longer-term evidence; while 6 studies on Ilex paraguariensis, Spinacia oleracea, Phaseolus vulgaris, Secale cereale, Sorghum bicolor and Plantago showed short-term evidence for suppressing appetite. No serious adverse events were reported. Despite some methodological concerns in the included studies, there is promising evidence for suppressing appetite with herbal medicines that needs to be confirmed in long-term clinical trials with adequate sample size and higher methodological quality with more attention to safety, effective dose and side effects.

**Abstract:**

A healthy skin is a reflection of overall wellness. In skin fungal infections are the most common skin disorders these infections affect 10-20% population worldwide and are seen to be more prevalent in tropical countries due to its hot and humid climate. Homoeopathy is one of the best modes of treatment to cure cases of skin diseases.


**Abstract:**

**Introduction:** Previous studies on laboratory animals have evaluated the effects of CGA (chlorogenic acids) rather than GCBE (green coffee bean extract), and few studies have been conducted on human models. Thus, the purpose of the present study was to assess the effect of GCBE consumption on serum oxidized LDL-cholesterol (OX-LDL) and total antioxidant capacity (TAC) on patients with dyslipidemia.

**Method:** In this randomized, placebo-controlled, clinical trial, 70 male participants (age range 30–55 years) were assigned from the outpatient clinic of Arvand Petrochemical Company in Mah-shahr, Ahwaz, Iran to use 800 mg/day GCBE supplements or placebo for 8 weeks. Serum TAC and OX-LDL were determined by enzyme-linked immunosorbent assay.

**Results:** Compared with the placebo, GCBE intake led to a significant reduction in OX-LDL (~31.18 ng/ml) (P-value = <0.001) and a significant increase in TAC (71.73 μmol/l) concentration (P-value = 0.029). In the intervention group, GCBE supplementation resulted in a significant reduction in Oxidized LDL of −16.08 ± 33.30 (ng/ml) (P-value = 0.006), compared to baseline.

**Conclusions:** The current trial showed that the intake of 800 mg per day of GCBE may have favorable effects on TAC, and OX-LDL in patients with dyslipidemia. However, further studies are required to confirm the veracity of these results.


**Abstract:**
**Introduction:** Perioperative symptoms such as pain, nausea and anxiety are often inadequately treated. We conducted a pragmatic trial to evaluate the impact of Complementary and Alternative Medicine (CAM) treatments on these symptoms, within the framework of a general surgery department that integrates CAM.

**Methods:** Patients ≥ 18 years referred to CAM treatments by surgical medical staff were allocated to standard of care with CAM treatment (CAM group) or without, according to patient preference and practitioner availability. CAM treatments included Acupuncture, Reflexology, or Guided Imagery. The primary outcome variable was the change from baseline in symptom severity, measured by Visual Analogue Scale (VAS). Patients and practitioners were asked to report any adverse effects associated with CAM treatments.

**Results:** A total of 1127 patients were enrolled, 916 undergoing 1214 CAM treatments and 211 controls. Socio-demographic characteristics were similar in both groups. Patients in the CAM group had more severe baseline symptoms. Symptom reduction was greater in the CAM group compared with controls, with a mean reduction in pain of $-2.17 \pm 2.4$ vs $-0.29 \pm 2$ ($P<0.0001$); nausea $-1.2 \pm 2.42$ vs $-0.3 \pm 1.94$ ($P<0.0001$); and anxiety $-2.23 \pm 2.76$ vs $-0.03 \pm 2.54$ ($P<0.0001$). Acupuncture was more effective for nausea control. No significant adverse events were reported with any of the CAM therapies.

**Conclusion:** CAM treatments provide additional relief to Standard Of Care (SOC) for perioperative symptoms. Larger randomized control trial studies with longer follow-ups are needed to confirm these benefits. The study is registered with clinical trials.gov at (NCT01733771).


**Abstract:**

If we can exactly match patients concern with the mind rubric, we can reach simillimum very accurately. During our free time, if we read mind chapter of repertory and esp Delusions chapter than this knowledge will be very useful. Whenever patient presents, it will be easy to relate with mind rubric and crack the case. This is beautifully demonstrated in this case.


**Abstract:**

**Introduction:** Mindful walking is a meditation practice that combines physical activity and mindfulness practice. Some mindful walking interventions expect four weeks of attendance (as compared with the traditional 8-week models of mindfulness-based interventions, or MBIs), a practice that could make MBIs more accessible to working-age adults. This
study examined whether a 4-week mindful walking intervention increased physical activity and improved mental health outcomes.

**Methods:** We conducted a randomized experiment among adults with inadequate physical activity (N = 38), whereby the intervention group received a four-week, one-hour-per-week mindful walking intervention and the control group received instructions to increase physical activity. Everyone in both groups received a wrist-worn step count device as participation incentive. Physical activity (as measured by the Rapid Assessment of Physical Activity questionnaire, RAPA) and other health outcomes were assessed with online surveys at baseline (T1), post-intervention (T2), and one month after the intervention (T3). Those mental health outcomes included perceived stress (Perceived Stress Scale), depression (Brief Edinburgh Depression Scale), and Mental Health Inventory (MHI). The primary outcome of device-measured step count was recorded at T1 and T2. Independent two-sample t-tests were used to compare the primary outcomes at T1. Generalized linear mixed models (GLMM) with a random intercept for each subject were used to compare the two groups on the primary outcomes at all time points. The independent variables in the model included a binary variable for group assignment (intervention vs. control), a 3-level categorical variable for time, and their interaction. Age, gender and race/ethnicity are used as covariates in the model. Estimated changes (either differences or ratios between outcomes at time points T1 and T2/T3) are reported to assess change within groups.

**Results:** Both groups exhibited significant improvements in the RAPA measures of physical activity and depression. However, between-group differences were not statistically significant. There was no within-group or between-group difference on device-measured step count, though both groups yielded an average daily step count close to the recommended level of 8,000 steps per day for older adults. The intervention group exhibited a significant reduction in perceived stress, and this reduction was significantly greater than that of the control group at T2 (p = .025) although the difference was insignificant at T3. No significant difference in MHI was found.

**Discussion:** While these adults with inadequate physical activity increased their physical activity, no significant between-group differences in physical activity were identified. Potential reasons for the lack of significant findings could be due to the ceiling effect (the step count device for everyone in both groups might have encouraged more activity in both groups), limited sample size and low-dose 4-week intervention used in this study. On the other hand, it is encouraging to see that this low-dose, short-duration 4-week intervention (as compared with those popular 8-week MBIs) achieved significantly greater stress reduction among the intervention group than among the control group, even though the between-group difference at one-month follow-up was statistically insignificant. Further studies with larger sample sizes and longer follow-up are needed to assess the possible benefits of these short-duration mindful walking interventions.

Abstract:
This article details about the skin manifestations as a mirror in internal systemic diseases, it is the sole duty of homoeopathic physician to find out the root cause of external manifestations of internal diseases rather than the suppressing of skin symptom by external applications. It’s how as we throw the house hold waste from inside to outside as the same human body which is affected with internal diseases which tries to throw the diseases from inner side to out as a skin symptoms that is how skin works as a mirror of internal deviation so when the skin symptoms starts to appear in chronic internal diseases after the administration of the similimum internally it is a good sign that the cure is taking place from center to periphery at this time just leave body to act itself to get complete cure instead of applying any external applications.


Abstract:

Introduction: Coronary artery disease is prevalent with high morbidity and coronary artery bypass grafting is one of its most important treatments. Anxiety and sleep disorders after surgery are very common and need appropriate control. The current study aimed to evaluate the efficacy of Melissa officinalis L. (Lemon Balm) for managing this problem.

Methods: A double-blind randomized placebo controlled clinical trial was conducted with 80 in-patients who underwent coronary artery bypass surgery. The patients were randomized into either the herbal medicine or the placebo group. Capsules containing 500 mg of Melissa officinalis L. dried leaf powder as herbal medicine or wheat starch as placebo were administered three times a day. Sleep quality and anxiety measures were the main outcomes and St Mary’s Hospital Sleep Quality and Hospital Anxiety Depression Scale were used questionnaires respectively.

Results: At baseline there were no significant differences in the anxiety scores between the two groups. After the intervention, anxiety scores were 7.15 ± 1.2 and 10.18 ± 3.1 in the herbal medicine and placebo groups respectively (P = 0.001). Moreover, the mean changes of sleep quality in the herbal medicine group was significantly higher than the placebo group; 14.40 ± 5.1 vs 7.52 ± 4.4 (P< 0.001).

Conclusion: The results of current study showed that seven-day treatment with 1.5 g/day dried leaf powder of Melissa officinalis appeared to reduce the
levels of anxiety and improve the sleep quality in patients after coronary artery bypass surgery, by 49% and 54% respectively.


Abstract:

**Objectives:** The objectives of this study were to identify: 1) the extent to which final year chiropractic students used components of person-centred care in a clinical setting; and 2) determine the effect of chiropractic students’ use of person-centred care on musculoskeletal pain.

**Design/setting:** An observational study was conducted at three Western Australian chiropractic teaching clinics.

**Interventions:** Pragmatic individualised chiropractic care was delivered to 108 adults who experienced non-specific spinal pain.

**Main outcome measures:** The instruments used in this study were the Consultation and Relational Empathy questionnaire, Picker Musculoskeletal Disorder Questionnaire, and Numerical Rating scale for Pain intensity.

**Results:** Participants experienced reductions in pain that exceeded the level required for minimal clinically reported improvement. In addition, high levels of empathy and patient-centred care were reported. Ceiling effects for the measures assessing empathy and patient-centred care precluded analyses examining the relationship between changes in pain intensity, empathy, and patient-centred care.

**Conclusions:** The participants in this study displayed very positive attitudes about most aspects of the chiropractic students’ person-centred care skills. Person-centred care processes for which there was considerable scope for improvement included advice about alternative treatment options, and the adaptation of lifestyle and workplace situations to alleviate pain and enhance health. Our findings also showed that the participants experienced clinically important improvement in pain. However, the skewed nature of our dataset precluded identifying whether the students’ person-centred care skills influenced such improvement.


Abstract:

Background: Traumatic facial palsy, whether accidental or iatrogenic, is a common cause of facial paralysis. Laser acupuncture therapy (LAT) is a non-invasive, pain-free method to stimulate traditional acupuncture points with non-thermal laser irradiation. Low-level laser therapy has proven beneficial in the regeneration of peripheral nerves. This case report describes the feasibility of this innovative treatment in a patient with a 12-year history of traumatic facial palsy and severe sequelae.

Case summary: A 52-year-old male presented with a severe left-sided facial paralysis that had lasted for 12 years. At initial presentation, the man could not fully close his left eye and had difficulty eating solid foods. The paralysis of his left-sided facial muscles had resulted in dysarthria. He was administered 30 LAT sessions in the Acupuncture Department of China Medical University Hospital, Taichung, Taiwan, over a 4-month period. His recovery was monitored by scores on the Facial Disability Index, the Sunnybrook Facial Nerve Grading System and measurements of the vertical palpebral distance in his left eye. Photographs were taken after every treatment. On the 10th treatment, a change in closure of the left eye was noticed and facial muscle strength was improved. After 22 treatments, the patient could fully close his left eye.

Conclusion: LAT significantly improved the sequelae of long-term facial paralysis in this patient. Large-scale prospective studies are needed to confirm this observation.


Abstract:

Objective: The purpose of this pragmatic controlled trial was to examine changes in psychological and occupational well-being in professionals who attended a yoga-based program.

Setting: The 5-day RISE (resilience, integration, self-awareness, engagement) program was delivered at the Kripalu Center for Yoga & Health. RISE included 5 h per day of yoga, meditation, lectures, and experiential activities.
Subjects: Adult professionals from education, corrections, and social service institutions were pragmatically assigned to the RISE group ($n = 61$) or a waitlist control group ($n = 60$).

Outcome measures: Measures of psychological and occupational well-being were completed before RISE (baseline), immediately after RISE (postprogram), and 2 months after RISE (follow-up). Analyses of covariance were conducted to compare change scores between groups.

Results: Eighty-two participants (RISE $n = 41$, control $n = 41$) completed baseline and postmeasures and were included in the analysis, and 57 (RISE $n = 27$, control $n = 30$) also completed the follow-up. Relative to controls, the RISE group reported improvements in stress ($p = 0.001$, $r^2 = 0.51$), resilience ($p = 0.028$, $r^2 = 0.34$), positive affect ($p = 0.001$, $r^2 = 0.52$), negative affect ($p = 0.001$, $r^2 = 0.52$), mindfulness ($p = 0.021$, $r^2 = 0.13$), and job satisfaction ($p = 0.034$, $r^2 = 0.08$) from baseline to postprogram. From baseline to follow-up, compared with controls the RISE group showed improvements in stress ($p = 0.001$, $r^2 = 0.33$), resilience ($p = 0.001$, $r^2 = 0.24$), positive affect ($p = 0.006$, $r^2 = 0.49$), negative affect ($p = 0.043$, $r^2 = 0.32$), mindfulness ($p = 0.001$, $r^2 = 0.28$), empowerment ($p = 0.005$, $r^2 = 0.20$), and self-compassion ($p = 0.011$, $r^2 = 0.19$).

Conclusions: The RISE program was associated with improvements in psychological and occupational well-being immediately after and 2 months after the program. Future research is needed to confirm these results.


Abstract:

Introduction: People use shiatsu for health maintenance and help with illness. Shiatsu is often considered safe, but there has been no published systematic review of its possible risks. The review aims to assess the evidence of safety and risk of harm from shiatsu.

Methods: All types of studies, independent of control and with any style of shiatsu will be eligible. Reports in any language will be included. Peer-reviewed studies and non-peer-reviewed literature will be handled in separate parts of the review. Electronic databases (including among others MEDLINE, AMED, Alt HealthWatch, Web of Science, CiNii) will be searched for identification of peer-reviewed publications. Hand-search will be used for non-peer-reviewed literature. Risk of bias will be assessed using RoB 2.0 in conjunction with McHarm (randomised trials), ROBINS:I in conjunction with McHarm (non-randomised studies), a modified PHARMA checklist (adverse reports). When appropriate, reporting bias will be assessed using ORBIT. The relevance of the described intervention to shiatsu will be based on clinical experience, using CARE for massage and bodywork and TIDieR. Root cause analysis of adverse events will consider Bradford Hill’s criteria in the light of clinical experience.
Results: Meta-analysis is not planned. Results for each study will be presented in tables. Relationships within and between studies will be explored. A theory about the safety profile of shiatsu will be developed. Identified incidents will be presented in a narrative way and tabular categories.

Conclusion: The relevance to various stakeholders will be highlighted and the issues occurring from the review will be explored.


Abstract:
Objective: The pathophysiology of atopic dermatitis (AD) involves a complex interplay between immune system dysfunction, genetics, and environmental factors. It is well known that nutritional status is essential to a proper functioning immune system, leading to a highly debated question regarding the role of dietary factors in the pathogenesis of AD. Food allergies and elimination diets have been broadly studied in atopy; however, less consideration has been given to how vitamins, minerals, and other micronutrients influence the risk for AD and severity of symptoms. This systematic review discusses evidence on how various micronutrients, including vitamins (C, E, and D) and trace minerals (zinc, selenium, iron, copper, magnesium, and strontium) are associated with AD, and how supplementation influence disease severity.

Design: A systematic search was conducted to identify the role that oral micronutrients have on AD. The authors reviewed 49 studies herein.

Results: While there are weak associations between vitamins C or E and AD, there is sufficient evidence to suggest that vitamin D supplementation provides benefit in AD patients. Deficiency of selenium and zinc may exacerbate AD. Current reports are not sufficient to confidently discern the role of other vitamins and trace minerals on AD.

Conclusions: Though oral micronutrients may play a role in AD, the current literature is limited, and there is a need for more comprehensive randomized controlled trials (RCTs) to truly decipher the role between oral micronutrients and AD.


Abstract:
**Objective:** To assess the effects and associated risks of Chinese herbal medicine (CHM) for diabetic foot ulcer (DFU).

**Methods:** We systematically searched seven electronic databases for randomized controlled trials (RCTs) about Chinese herbal medicines for treating diabetic foot ulcers. The methodological quality of RCTs was assessed by the Cochrane risk of bias tool. Data was synthesized using review manager (RevMan) 5.3. Meta-analysis was conducted if the data were available. A summary of finding table was generated by The GRADEpro Guideline Development Tool (GDT) online.

**Results:** Forty-nine RCTs, all conducted in China, involving 3646 participants were included. Most of the included trials had unclear or high risk of bias. Twenty-six trials could be pooled in five Meta-analyses, the remaining trials could not be pooled due to the obvious clinical heterogeneity. Only low evidence showed CHM therapy may have 42%–60.4% participants healed completely after treatment, approximately twice (RR 1.42–1.76) as much as the healed rates in conventional therapy (or plus hot water foot bath) group. Majority of the included trials reported benefit of CHM group on shortening healing time (4–23 days) and reducing ulcer wound size (at least 2 cm²). No serious adverse events were reported related to the medication in all trials.

**Conclusion:** Weak evidence showed benefit of CHM as add-on treatment of conventional therapy on increasing number of ulcer heals in patients with DFU. That’s about twice the healing rate of the conventional treatment (or plus hot water foot bath) group. With insufficient information, we could not draw confirmative conclusion on safety of CHM administration. These findings need to be tested in further large, rigorous trials.


**Abstract:**

**Background:** Moderate-severe acne treatment involves the use of isotretinoin and antibiotics as first-line therapeutics; however, these drugs have serious
side effects. Fire needle therapy, which is widely used in China, has shown good clinical efficacy for treating moderate-severe acne; moreover, it has fewer side effects, hence, it can be used as a primary treatment (as an alternative to pharmaceutical medications) or in combination with pharmaceutical medications for clinical treatment. However, current clinical evidence regarding its use has not been comprehensively evaluated.

**Methods:** We systematically searched several databases, including PubMed, Embase, Cochrane Central Register of Controlled Trials, China Network Knowledge Infrastructure (CNKI), China Biomedical Literature Service System (SinoMed), China Science and Technology Journal Database (CQVIP), and Wanfang Data Knowledge Service Platform, from their inception time to November 22, 2018. Randomized controlled trials conducted to compare the efficacy, acne recurrence, and adverse events associated with fire needle therapy alone, or in combination with Chinese herbs or conventional pharmaceutical medication, to those of pharmaceutical treatment were selected. RevMan 5.3 software was used to calculate risk ratio (RR) with a 95% confidence interval (CI).

**Results:** Ten trials, with a total of 904 participants, met the inclusion criteria. Meta-analyses showed that fire needle treatment with clindamycin or oral isotretinoin treatment had advantages over pharmaceutical medications alone in the treatment of moderate-severe acne [RR = 2.18, 95% CI (1.19, 3.99), P = 0.03 random model; I² = 72%]. Moreover, the use of fire needle therapy alone in the treatment of moderate-severe acne had a better effect than pharmaceutical medications, regardless of the type of pharmaceutical medication used [RR = 2.32, 95% CI (1.77, 3.03), P < 0.00001 random model; I² = 59%]. In terms of recurrence rate, there was no significant difference between fire needle and pharmaceutical medication groups [RR = 0.78, 95% CI (0.54, 1.14), P = 0.20 fixed-effect model; I² = 0%]. In addition, the use of fire needles was associated with few adverse reactions, such as burning and tingling; furthermore, the adverse reactions were transient.

**Conclusion:** Fire needle therapy alone or combined with other treatments is effective for moderate-severe acne. However, further large-scale, rigorously designed trials are needed to confirm these findings.


**Abstract:**

**Background:** This study aimed to determine the effectiveness of music listening for procedural pain relief using two different observational pain tools during endotracheal suctioning.

**Materials and Methods:** This study was a randomized controlled trial. The sample of the study included 98 patients with mechanical ventilation support who met the selection criteria. The patients were randomly assigned to control
and music therapy groups. Patients in the control group were routinely suctioned as usual. Patients in the music group received music therapy 20 min before, during, and 20 min after endotracheal suctioning. The primary outcome was the pain relief during suctioning.

**Results:** Forty patients in each arm completed the study. Pain scores in the Critical Care Pain Observation Tool and Behavioral Pain Scale were lower in the music group than in the control group during endotracheal suctioning (group: \( F = 14.85, p = 0.000; F = 9.04, p = 0.000 \), respectively). It was also found to be a significant interaction effect between the groups and time (group \( \times \) time: \( F = 17.35, p = 0.000; F = 18.00, p = 0.000 \), respectively).

**Conclusion:** The Critical Care Pain Observation Tool and Behavioral Pain Scale in the current study generally demonstrated similar pain scores during the painful procedure. Our findings support that music therapy may act as a nonpharmacological therapy to relieve procedural pain in patients on mechanical ventilation.


**Abstract:**

Increasing sales of medicinal plants as supplements or health foods continue to indicate widespread self-medication. We conducted a survey on users’ views on obtaining information on herbal medicines and their experiences and opinions about their use. Responses over one-year period (01.08.2015–31.07.2016) were analysed.

157 participants took part (87% aged 45–64y, and 13% >65y). 80% participants used medicinal plants for multiple health benefits [i.e. health protection (74%), disease prevention (38%) and treatment (49%)]. 95% believed in the medicinal powers of plants. Information regarding use of medicinal plants was predominantly based on books (57%), the internet (53%), friends, colleagues or neighbours (51%) and health practitioners (42%). 51% of participants felt herbs were safe (51%) with less side effects (55%) than pharmaceutical medicines. 24% of medicinal plant users informed their medical doctor, with majority of informed medical professional (47%) accepting the use of medicinal plants.

This pilot survey provides new and valuable information for use in designing future more comprehensive surveys to provide essential information about the use of herbal medicines by the general population and health care providers’ attitudes in the UK.

Abstract:

L-carnitine infusion has been proven to reduce fasting-induced fatigue and hunger in patients with metabolic syndrome in our former study. However, the association between L-carnitine and clinical outcomes of fasting therapy is yet to be investigated. In this study, data from 192 patients who finished fasting therapy from September 2008 to July 2018 were reviewed, among which 142 patients received L-carnitine infusion in fasting regimen. Propensity matching was used to overcome retrospective bias. Patients’ anthropometric measurements and metabolic markers were evaluated. After propensity matching, 40 patients were included in each group. Weight (-4.05 ± 1.65 kg vs -3.25 ± 1.68 kg, $P = 0.031$) and BMI (-1.51±0.61 kg/m² vs -1.20 ± 0.62 kg/m², $P = 0.036$) decreased in both groups, but significantly more in L-carnitine group, while diastolic blood pressure (-1.67±9.82 mmHg vs -6.21±8.83 mmHg, $P = 0.043$) and triglycerides (-0.18±0.63 mmol/L vs -1.05±1.70 mmol/L, $P = 0.007$) decreased significantly more in non-L-carnitine group compared between groups, blood glucose did not differ significantly between groups. L-carnitine can boost the positive effects of fasting therapy on weight loss and maintain the stability of blood pressure.


Abstract:

Low-risk skin cancers and precancers are common skin ailments that primarily affect fair skinned individuals in areas of skin with high sun exposure. Currently the primary treatments available for these types of lesions include surgery and cryotherapy, with the less common use of chemotherapeutic agents either topically or orally. These treatments tend to leave lasting scars and have a high rate of recurrence. Several products derived from plants including oleogel from Betula spp. (birch) and ingenol mebutate from Euphorbia peplus (garden spurge) have demonstrated effectiveness as treatments for actinic keratoses, with minimal side effects, scarring, and recurrence. Other herbs with preclinical evidence are discussed, including Hypericum perforatum (St. John’s wort), Camellia sinensis (green tea), Curcuma longa (turmeric), and Vitis vinifera (grape seed). Sun damage is the primary cause of these types of skin lesions; various botanical interventions for photoprotection are reviewed.
Allied System


**Abstract:**

**Background:** Stroke thrombolysis with alteplase is currently recommended 0–4·5 h after stroke onset. We aimed to determine whether perfusion imaging can identify patients with salvageable brain tissue with symptoms 4·5 h or more from stroke onset or with symptoms on waking who might benefit from thrombolysis.

**Methods:** In this systematic review and meta-analysis of individual patient data, we searched PubMed for randomised trials published in English between Jan 1, 2006, and March 1, 2019. We also reviewed the reference list of a previous systematic review of thrombolysis and searched ClinicalTrials.gov for interventional studies of ischaemic stroke. Studies of alteplase versus placebo in patients (aged ≥18 years) with ischaemic stroke treated more than 4·5 h after onset, or with wake-up stroke, who were imaged with perfusion-diffusion MRI or CT perfusion were eligible for inclusion. The primary outcome was excellent functional outcome (modified Rankin Scale [mRS] score 0–1) at 3 months, adjusted for baseline age and National Institutes of Health Stroke Scale score, using mixed-effects logistic regression models. This study is registered with PROSPERO, number CRD42019128036.

**Findings:** We identified three trials that met eligibility criteria: EXTEND, ECASS4-EXTEND, and EPITHET. Of the 414 patients included in the three trials, 213 (51%) were assigned to receive alteplase and 201 (49%) were assigned to receive placebo. Overall, 211 patients in the alteplase group and 199 patients in the placebo group had mRS assessment data
at 3 months and thus were included in the analysis of the primary outcome. 76 (36%) of 211 patients in the alteplase group and 58 (29%) of 199 patients in the placebo group had achieved excellent functional outcome at 3 months (adjusted odds ratio [OR] 1·86, 95% CI 1·15–2·99, p=0·011). Symptomatic intracerebral haemorrhage was more common in the alteplase group than the placebo group (ten [5%] of 213 patients vs one [<1%] of 201 patients in the placebo group; adjusted OR 9·7, 95% CI 1·23–76·55, p=0·031). 29 (14%) of 213 patients in the alteplase group and 18 (9%) of 201 patients in the placebo group died (adjusted OR 1·55, 0·81–2·96, p=0·66).

**Interpretation:** Patients with ischaemic stroke 4-5–9 h from stroke onset or wake-up stroke with salvageable brain tissue who were treated with alteplase achieved better functional outcomes than did patients given placebo. The rate of symptomatic intracerebral haemorrhage was higher with alteplase, but this increase did not negate the overall net benefit of thrombolysis.

**Funding:** None.

**Caring for patients who have been tortured in detention. *Lancet* 2019; 393(10191): 2564p.**


**Chatterjee Patralekha. No cause identified for death of children in Bihar, India. *Lancet* 2019; 393(10191): 2578p.**

**Chen Yu-Pei, Chan Anthony T C, Le Quynh-Thu, Blanchard Pierre et al. Nasopharyngeal carcinoma. *Lancet* 2019; 393(10192): 64-80p.**

**Abstract:**

Nasopharyngeal carcinoma is characterised by distinct geographical distribution and is particularly prevalent in east and southeast Asia. Epidemiological trends in the past decade have shown that its incidence has declined gradually but progressively, and mortality has been reduced substantially. These findings probably reflect lifestyle and environmental changes, enhanced understanding of the pathogenesis and risk factors, population screening, advancements in imaging techniques, and individualised comprehensive chemoradiotherapy strategies. In particular, plasma Epstein-Barr virus (EBV) DNA has been used for population screening, prognostication, predicting treatment response for therapeutic adaptation, and disease surveillance. Moreover, the widespread application of intensity-modulated radiotherapy and
optimisation of chemotherapy strategies (induction, concurrent, adjuvant) have contributed to improved survival with reduced toxicities. Among the existing developments in novel therapeutics, immune checkpoint therapies have achieved breakthroughs for treating recurrent or metastatic disease and represent a promising future direction in nasopharyngeal carcinoma.

**Creating respectful health care for trans patients.** *Lancet 2019; 393(10192): 2p.*

**Cruz-Jentoft Alfonso J, Sayer Avan A. Sarcopenia.** *Lancet 2019; 393(10191): 2636-646p.*

**Abstract:**

Sarcopenia is a progressive and generalised skeletal muscle disorder involving the accelerated loss of muscle mass and function that is associated with increased adverse outcomes including falls, functional decline, frailty, and mortality. It occurs commonly as an age-related process in older people, influenced not only by contemporaneous risk factors, but also by genetic and lifestyle factors operating across the life course. It can also occur in mid-life in association with a range of conditions. Sarcopenia has become the focus of intense research aiming to translate current knowledge about its pathophysiology into improved diagnosis and treatment, with particular interest in the development of biomarkers, nutritional interventions, and drugs to augment the beneficial effects of resistance exercise. Designing effective preventive strategies that people can apply during their lifetime is of primary concern. Diagnosis, treatment, and prevention of sarcopenia is likely to become part of routine clinical practice.


**Abstract:**

**Background:** Use of oral live-attenuated polio vaccines (OPV), and injected inactivated polio vaccines (IPV) has almost achieved global eradication of wild polio viruses. To address the goals of achieving and maintaining global eradication and minimising the risk of outbreaks of vaccine-derived polioviruses, we tested novel monovalent oral type-2 poliovirus (OPV2) vaccine candidates that are genetically more stable than existing OPVs, with a lower risk of reversion to neurovirulence. Our study represents the first in-human testing of these two novel OPV2
candidates. We aimed to evaluate the safety and immunogenicity of these vaccines, the presence and extent of faecal shedding, and the neurovirulence of shed virus.

**Methods:** In this double-blind, single-centre phase 1 trial, we isolated participants in a purpose-built containment facility at the University of Antwerp Hospital (Antwerp, Belgium), to minimise the risk of environmental release of the novel OPV2 candidates. Participants, who were recruited by local advertising, were adults (aged 18–50 years) in good health who had previously been vaccinated with IPV, and who would not have any contact with immunosuppressed or unvaccinated people for the duration of faecal shedding at the end of the study. The first participant randomly chose an envelope containing the name of a vaccine candidate, and this determined their allocation; the next 14 participants to be enrolled in the study were sequentially allocated to this group and received the same vaccine. The subsequent 15 participants enrolled after this group were allocated to receive the other vaccine. Participants and the study staff were masked to vaccine groups until the end of the study period. Participants each received a single dose of one vaccine candidate (candidate 1, S2/cre5/S15domV/rec1/hifi3; or candidate 2, S2/S15domV/CpG40), and they were monitored for adverse events, immune responses, and faecal shedding of the vaccine virus for 28 days. Shed virus isolates were tested for the genetic stability of attenuation. The primary outcomes were the incidence and type of serious and severe adverse events, the proportion of participants showing viral shedding in their stools, the time to cessation of viral shedding, the cell culture infective dose of shed virus in virus-positive stools, and a combined index of the prevalence, duration, and quantity of viral shedding in all participants. This study is registered with EudraCT, number 2017-000908-21 and ClinicalTrials.gov, number NCT03430349.

**Findings:** Between May 22 and Aug 22, 2017, 48 volunteers were screened, of whom 15 (31%) volunteers were excluded for reasons relating to the inclusion or exclusion criteria, three (6%) volunteers were not treated because of restrictions to the number of participants in each group, and 30 (63%) volunteers were sequentially allocated to groups (15 participants per group). Both novel OPV2 candidates were immunogenic and increased the median blood titre of serum neutralising antibodies; all participants were seroprotected after vaccination. Both candidates had acceptable tolerability, and no serious adverse events occurred during the study. However, severe events were reported in six (40%) participants receiving candidate 1 (eight events) and nine (60%) participants receiving candidate 2 (12 events); most of these events were increased blood creatinine phosphokinase but were not accompanied by clinical signs or symptoms. Vaccine virus was detected in the stools of
15 (100%) participants receiving vaccine candidate 1 and 13 (87%) participants receiving vaccine candidate 2. Vaccine poliovirus shedding stopped at a median of 23 days (IQR 15–36) after candidate 1 administration and 12 days (1–23) after candidate 2 administration. Total shedding, described by the estimated median shedding index (50% cell culture infective dose/g), was observed to be greater with candidate 1 than candidate 2 across all participants (2.8 [95% CI 1.8–3.5] vs 1.0 [0.7–1.6]). Reversion to neurovirulence, assessed as paralysis of transgenic mice, was low in isolates from those vaccinated with both candidates, and sequencing of shed virus indicated that there was no loss of attenuation in domain V of the 5ʹ-untranslated region, the primary site of reversion in Sabin OPV.

**Interpretation:** We found that the novel OPV2 candidates were safe and immunogenic in IPV-immunised adults, and our data support the further development of these vaccines to potentially be used for maintaining global eradication of neurovirulent type-2 polioviruses.

**Funding:** Bill & Melinda Gates Foundation.


**Abstract:**

Adult spinal deformity affects the thoracic or thoracolumbar spine throughout the ageing process. Although adolescent spinal deformities taken into adulthood are not uncommon, the most usual causes of spinal deformity in adults are iatrogenic flatback and degenerative scoliosis. Given its prevalence in the expanding portion of the global population aged older than 65 years, the disorder is of growing interest in health
care. Physical examination, with a focus on gait and posture, along with radiographical assessment are primarily used and integrated with risk stratification indices to establish optimal treatment planning. Although non-operative treatment is regarded as the first-line response, surgical outcomes are considerably favourable. Global disparities exist in both the assessment and treatment of adults with spinal deformity across countries of varying incomes, which represents an area requiring further investigation. This Seminar presents evidence and knowledge that represent the evolution of data related to spinal deformity in adults over the past several decades.


Abstract:
Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by the loss of self-tolerance and formation of nuclear autoantigens and immune complexes resulting in inflammation of multiple organs. The clinical presentation of SLE is heterogeneous, can involve one or more organs, including the skin, kidneys, joints, and nervous system, and take a chronic or relapsing and remitting disease course. SLE is most common in women and in those of non-white ethnicity. Because of the multitude of presentations, manifestations, and serological abnormalities in patients with SLE, diagnosis can be challenging. Therapeutic approaches predominantly involve immunomodulation and immunosuppression and are targeted to the specific organ manifestation, with the aim of achieving low disease activity. Despite many treatment advances and improved diagnostics, SLE continues to cause substantial morbidity and premature mortality. Current management strategies, although helpful, are limited by high failure rates and toxicity. An overreliance on corticosteroid therapy contributes to much of the long-term organ damage. In this Seminar, we outline the classification criteria for SLE, current treatment strategies and medications, the evidence supporting their use, and explore potential future therapies.


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Abstract:

Background: Adjuvant trastuzumab significantly improves outcomes for patients with HER2-positive early breast cancer. The standard treatment duration is 12 months but shorter treatment could provide similar efficacy while reducing toxicities and cost. We aimed to investigate whether 6-month adjuvant trastuzumab treatment is non-inferior to the standard 12-month treatment regarding disease-free survival.

Methods: This study is an open-label, randomised phase 3 non-inferiority trial. Patients were recruited from 152 centres in the UK. We randomly assigned patients with HER2-positive early breast cancer, aged 18 years or older, and with a clear indication for chemotherapy, by a computerised minimisation process (1:1), to receive either 6-month or 12-month trastuzumab delivered every 3 weeks intravenously (loading dose of 8 mg/kg followed by maintenance doses of 6 mg/kg) or subcutaneously (600 mg), given in combination with chemotherapy (concurrently or sequentially). The primary endpoint was disease-free survival, analysed by intention to treat, with a non-inferiority margin of 3% for 4-year disease-free survival. Safety was analysed in all patients
who received trastuzumab. This trial is registered with EudraCT (number 2006–007018–39), ISRCTN (number 52968807), and ClinicalTrials.gov (number NCT00712140).

**Findings:** Between Oct 4, 2007, and July 31, 2015, 2045 patients were assigned to 12-month trastuzumab treatment and 2044 to 6-month treatment (one patient was excluded because they were double randomised). Median follow-up was 5·4 years (IQR 3·6–6·7) for both treatment groups, during which a disease-free survival event occurred in 265 (13%) of 2043 patients in the 6-month group and 247 (12%) of 2045 patients in the 12-month group. 4-year disease-free survival was 89·4% (95% CI 87·9–90·7) in the 6-month group and 89·8% (88·3–91·1) in the 12-month group (hazard ratio 1·07 [90% CI 0·93–1·24], non-inferiority \( p=0·011 \)), showing non-inferiority of the 6-month treatment. 6-month trastuzumab treatment resulted in fewer patients reporting severe adverse events (373 [19%] of 1939 patients vs 459 [24%] of 1894 patients, \( p=0·0002 \)) or stopping early because of cardiotoxicity (61 [3%] of 1939 patients vs 146 [8%] of 1894 patients, \( p<0·0001 \)).

**Interpretation:** We have shown that 6-month trastuzumab treatment is non-inferior to 12-month treatment in patients with HER2-positive early breast cancer, with less cardiotoxicity and fewer severe adverse events. These results support consideration of reduced duration trastuzumab for women at similar risk of recurrence as to those included in the trial.

**Funding:** UK National Institute for Health Research, Health Technology Assessment Programme.


Abstract:
Objective: Description of recruitment methods and lessons learned in a randomized controlled trial of underserved patients using an integrative medical group visits intervention.

Methods: Comparison of the demographic characteristics of participants screened and consented to the study as well as description of recruitment methods used.

Outcome Measures: This paper examines the characteristics of patients who were eligible compared to those who were not, characteristics of patients at the different sites, and patient characteristics over time (by comparing various cohorts) based on our experiences recruiting underserved patients.

Results: We screened 338 patients, with 205 (60.6%) meeting eligibility criteria and 159 patients randomized and consented. 133 patients were found ineligible, with the most common reasons being low depression scores (n = 20), manic symptoms (n = 20), and psychotic symptoms (n = 19), and alcohol use (n = 15). We found demographic differences in patients recruited by different methods and at different sites- patients referred by provider letter were older than those referred by self-referral or provider referral (mean age/SD vs. mean age/SD, p = 0.0001). For site-specific differences, patients at DH were older (53 SD = 12.3) than those at the Boston Medical Center (49 SD = 11.3) and CSHC (p = 0.048) in pair-wise comparisons. Patients at DH were also more likely to be white (25%) as compared to BMC (18%) and DH (7%), while those at CSHC were more likely to be black (70%) (p = 0.008).


Abstract:
The Sustainable Development Goals offer the global health community a strategic opportunity to promote human rights, advance gender equality, and achieve health for all. The inability of the health sector to accelerate progress on a range of health outcomes brings into sharp focus the substantial impact of gender inequalities and restrictive gender norms on health risks and behaviours. In this paper, the fifth in a Series on gender equality, norms, and health, we draw on evidence to dispel three myths on gender and health and describe persistent barriers to progress. We propose an agenda for action to reduce gender inequality and shift gender norms for improved health outcomes, calling on leaders in national governments, global health institutions, civil society organisations, academic settings, and the corporate sector to focus on health outcomes and engage actors across sectors to achieve them; reform the workplace and workforce to be more gender-equitable; fill gaps in data and eliminate gender bias in research; fund civil-society actors and social movements; and strengthen accountability mechanisms.


Abstract:

Background: Three different glucagon-like peptide-1 (GLP-1) receptor agonists reduce cardiovascular outcomes in people with type 2 diabetes at high cardiovascular risk with high glycated haemoglobin A1c (HbA1c) concentrations. We assessed the effect of the GLP-1 receptor agonist dulaglutide on major adverse cardiovascular events when added to the existing antihyperglycaemic regimens of individuals with type 2 diabetes with and without previous cardiovascular disease and a wide range of glycaemic control.
Methods: This multicentre, randomised, double-blind, placebo-controlled trial was done at 371 sites in 24 countries. Men and women aged at least 50 years with type 2 diabetes who had either a previous cardiovascular event or cardiovascular risk factors were randomly assigned (1:1) to either weekly subcutaneous injection of dulaglutide (1·5 mg) or placebo. Randomisation was done by a computer-generated random code with stratification by site. All investigators and participants were masked to treatment assignment. Participants were followed up at least every 6 months for incident cardiovascular and other serious clinical outcomes. The primary outcome was the first occurrence of the composite endpoint of non-fatal myocardial infarction, non-fatal stroke, or death from cardiovascular causes (including unknown causes), which was assessed in the intention-to-treat population. This study is registered with ClinicalTrials.gov, number NCT01394952.

Findings: Between Aug 18, 2011, and Aug 14, 2013, 9901 participants (mean age 66·2 years [SD 6·5], median HbA1c 7·2% [IQR 6·6–8·1], 4589 [46·3%] women) were enrolled and randomly assigned to receive dulaglutide (n=4949) or placebo (n=4952). During a median follow-up of 5·4 years (IQR 5·1–5·9), the primary composite outcome occurred in 594 (12·0%) participants at an incidence rate of 2·4 per 100 person-years in the dulaglutide group and in 663 (13·4%) participants at an incidence rate of 2·7 per 100 person-years in the placebo group (hazard ratio [HR] 0·88, 95% CI 0·79–0·99; p=0·026). All-cause mortality did not differ between groups (536 [10·8%] in the dulaglutide group vs 592 [12·0%] in the placebo group; HR 0·90, 95% CI 0·80–1·01; p=0·067). 2347 (47·4%) participants assigned to dulaglutide reported a gastrointestinal adverse event during follow-up compared with 1687 (34·1%) participants assigned to placebo (p<0·0001).

Interpretation: Dulaglutide could be considered for the management of glycaemic control in middle-aged and older people with type 2 diabetes with either previous cardiovascular disease or cardiovascular risk factors.

Funding: Eli Lilly and Company.

Abstract:

Background: International guidelines advise laparoscopic cholecystectomy to treat symptomatic, uncomplicated gallstones. Usual care regarding cholecystectomy is associated with practice variation and persistent post-cholecystectomy pain in 10–41% of patients. We aimed to compare the non-inferiority of a restrictive strategy with stepwise selection with usual care to assess (in)efficient use of cholecystectomy.

Methods: We did a multicentre, randomised, parallel-arm, non-inferiority study in 24 academic and non-academic hospitals in the Netherlands. We enrolled patients aged 18–95 years with abdominal pain and ultrasound-proven gallstones or sludge. Patients were randomly assigned (1:1) to either usual care in which selection for cholecystectomy was left to the discretion of the surgeon, or a restrictive strategy with stepwise selection for cholecystectomy. For the restrictive strategy, cholecystectomy was advised for patients who fulfilled all five prespecified criteria of the triage instrument: 1) severe pain attacks, 2) pain lasting 15–30 min or longer, 3) pain located in epigastrium or right upper quadrant, 4) pain radiating to the back, and 5) a positive pain response to simple analgesics. Randomisation was done with an online program, implemented into a web-based application using blocks of variable sizes, and stratified for centre (academic versus non-academic and a high vs low number of patients), sex, and body-mass index. Physicians and patients were masked for study-arm allocation until after completion of the triage instrument. The primary, non-inferiority, patient-reported endpoint was the proportion of patients who were pain-free at 12 months' follow-up, analysed by intention to treat and per protocol. A 5% non-inferiority margin was chosen, based on the estimated clinically relevant difference. Safety analyses were also done in the intention-to-treat population. This trial is registered at the Netherlands National Trial Register, number NTR4022.

Findings: Between Feb 5, 2014, and April 25, 2017, we included 1067 patients for analysis: 537 assigned to usual care and 530 to the restrictive strategy. At 12 months' follow-up 298 patients (56%; 95% CI, 52·0–60·4) were pain-free in the restrictive strategy group, compared with 321 patients (60%, 55·6–63·8) in usual care. Non-inferiority was not shown (difference 3·6%; one-sided 95% lower CI −8·6%; p_{non-inferiority}=0·316). According to a secondary endpoint analysis, the
Restrictive strategy resulted in significantly fewer cholecystectomies than usual care (358 [68%] of 529 vs 404 [75%] of 536; p=0.01). There were no between-group differences in trial-related gallstone complications (40 patients [8%] of 529 in usual care vs 38 [7%] of 536 in restrictive strategy; p=0.16) and surgical complications (74 [21%] of 358 vs 88 [22%] of 404, p=0.77), or in non-trial-related serious adverse events (27 [5%] of 529 vs 29 [5%] of 526).

**Interpretation:** Suboptimal pain reduction in patients with gallstones and abdominal pain was noted with both usual care and following a restrictive strategy for selection for cholecystectomy. However, the restrictive strategy was associated with fewer cholecystectomies. The findings should encourage physicians involved in the care of patients with gallstones to rethink cholecystectomy, and to be more careful in advising a surgical approach in patients with gallstones and abdominal symptoms.

**Funding:** The Netherlands Organization for Health Research and Development, and CZ healthcare insurance.


**Abstract:**

**Background:** Two glucagon-like peptide-1 (GLP-1) receptor agonists reduced renal outcomes in people with type 2 diabetes at risk for cardiovascular disease. We assessed the long-term effect of the GLP-1 receptor agonist dulaglutide on renal outcomes in an exploratory analysis of the REWIND trial of the effect of dulaglutide on cardiovascular disease.

**Methods:** REWIND was a multicentre, randomised, double-blind, placebo-controlled trial at 371 sites in 24 countries. Men and women aged at least 50 years with type 2 diabetes who had either a previous cardiovascular event or cardiovascular risk factors were randomly assigned (1:1) to either weekly subcutaneous injection of dulaglutide (1.5 mg) or placebo and followed up at least every 6 months for outcomes. Urinary albumin-to-creatinine ratios (UACRs) and estimated glomerular filtration rates (eGFRs) were estimated from urine and serum values measured in local laboratories every 12 months. The primary outcome (first occurrence of the composite endpoint of non-fatal myocardial infarction, non-fatal stroke, or death from cardiovascular causes),
secondary outcomes (including a composite microvascular outcome), and safety outcomes of this trial have been reported elsewhere. In this exploratory analysis, we investigate the renal component of the composite microvascular outcome, defined as the first occurrence of new macroalbuminuria (UACR >33·9 mg/mmol), a sustained decline in eGFR of 30% or more from baseline, or chronic renal replacement therapy. Analyses were by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT01394952.

**Findings:** Between Aug 18, 2011, and Aug 14, 2013, 9901 participants were enrolled and randomly assigned to receive dulaglutide (n=4949) or placebo (n=4952). At baseline, 791 (7·9%) had macroalbuminuria and mean eGFR was 76·9 mL/min per 1·73 m² (SD 22·7). During a median follow-up of 5·4 years (IQR 5·1–5·9) comprising 51 820 person-years, the renal outcome developed in 848 (17·1%) participants at an incidence rate of 3·5 per 100 person-years in the dulaglutide group and in 970 (19·6%) participants at an incidence rate of 4·1 per 100 person-years in the placebo group (hazard ratio [HR] 0·85, 95% CI 0·77–0·93; p=0·0004). The clearest effect was for new macroalbuminuria (HR 0·77, 95% CI 0·68–0·87; p<0·0001), with HRs of 0·89 (0·78–1·01; p=0·066) for sustained decline in eGFR of 30% or more and 0·75 (0·39–1·44; p=0·39) for chronic renal replacement therapy.

**Interpretation:** Long-term use of dulaglutide was associated with reduced composite renal outcomes in people with type 2 diabetes.

**Funding:** Eli Lilly and Company.


**Abstract:**

Gender is not accurately captured by the traditional male and female dichotomy of sex. Instead, it is a complex social system that structures the life experience of all human beings. This paper, the first in a Series of five papers, investigates the relationships between gender inequality, restrictive gender norms, and health and wellbeing. Building upon past work, we offer a consolidated conceptual framework that shows how individuals born biologically male or female develop into gendered beings,
and how sexism and patriarchy intersect with other forms of discrimination, such as racism, classism, and homophobia, to structure pathways to poor health. We discuss the ample evidence showing the far-reaching consequences of these pathways, including how gender inequality and restrictive gender norms impact health through differential exposures, health-related behaviours and access to care, as well as how gender-biased health research and health-care systems reinforce and reproduce gender inequalities, with serious implications for health. The cumulative consequences of structured disadvantage, mediated through discriminatory laws, policies, and institutions, as well as diet, stress, substance use, and environmental toxins, have triggered important discussions about the role of social injustice in the creation and maintenance of health inequities, especially along racial and socioeconomic lines. This Series paper raises the parallel question of whether discrimination based on gender likewise becomes embodied, with negative consequences for health. For decades, advocates have worked to eliminate gender discrimination in global health, with only modest success. A new plan and new political commitment are needed if these global health aspirations and the wider Sustainable Development Goals of the UN are to be achieved.


**Abstract:**

Evidence that gender inequalities and restrictive norms adversely affect health is extensive; however, far less research has focused on testing solutions. We first comprehensively reviewed the peer-reviewed and grey literature for rigorously evaluated programmes that aimed to reduce gender inequality and restrictive gender norms and improve health. We identified four mutually reinforcing factors underpinning change: (1) multisectoral action, (2) multilevel, multistakeholder involvement, (3) diversified programming, and (4) social participation and empowerment. Following this review, because little research has investigated the effects of national-level law and policy reforms, we conducted original quasi-experimental studies on laws and policies related to education, work, and income, all social determinants of health in which deep gender inequalities exist. We examined whether the laws and policies significantly affected health outcomes and gender norms, and whether law-induced and policy-induced changes in gender norms mediated the
health effects, in areas for which longitudinal data existed. Laws and policies that made primary education tuition-free (13 intervention countries with the law and/or policy and ten control countries without) and that provided paid maternity and parental leave (seven intervention and 15 control countries) significantly improved women’s and their children’s health (odds ratios [OR] of 1·16–2·10, depending on health outcome) and gender equality in household decision making (OR 1·46 for tuition-free and 1·45 for paid maternity and parental leave) as a proxy indicator of gender norms. Increased equality partially mediated the positive effects on health outcomes. We conclude by discussing examples of how improved governance can support gender-equitable laws, policies, and programmes, immediate next steps, and future research needs.


Abstract:

Background: A phase 2 trial showed improved progression-free survival for atezolizumab plus bevacizumab versus sunitinib in patients with metastatic renal cell carcinoma who express programmed death-ligand 1 (PD-L1). Here, we report results of IMmotion151, a phase 3 trial comparing atezolizumab plus bevacizumab versus sunitinib in first-line metastatic renal cell carcinoma.

Methods: In this multicentre, open-label, phase 3, randomised controlled trial, patients with a component of clear cell or sarcomatoid histology and who were previously untreated, were recruited from 152 academic medical centres and community oncology practices in 21 countries, mainly in Europe, North America, and the Asia-Pacific region, and were randomly assigned 1:1 to either atezolizumab 1200 mg plus bevacizumab 15 mg/kg intravenously once every 3 weeks or sunitinib 50 mg orally once daily for 4 weeks on, 2 weeks off. A permuted-block randomisation (block size of 4) was applied to obtain a balanced assignment to each treatment group with respect to the stratification factors. Study investigators and participants were not masked to treatment allocation. Patients, investigators, independent radiology committee members, and the sponsor were masked to PD-L1 expression status. Co-primary endpoints were investigator-assessed progression-free survival in the PD-L1 positive population and overall survival in the intention-to-treat (ITT) population. This trial is registered with ClinicalTrials.gov, number NCT02420821.
Findings: Of 915 patients enrolled between May 20, 2015, and Oct 12, 2016, 454 were randomly assigned to the atezolizumab plus bevacizumab group and 461 to the sunitinib group. 362 (40%) of 915 patients had PD-L1 positive disease. Median follow-up was 15 months at the primary progression-free survival analysis and 24 months at the overall survival interim analysis. In the PD-L1 positive population, the median progression-free survival was 11·2 months in the atezolizumab plus bevacizumab group versus 7·7 months in the sunitinib group (hazard ratio [HR] 0·74 [95% CI 0·57–0·96]; p=0·0217). In the ITT population, median overall survival had an HR of 0·93 (0·76–1·14) and the results did not cross the significance boundary at the interim analysis. 182 (40%) of 451 patients in the atezolizumab plus bevacizumab group and 240 (54%) of 446 patients in the sunitinib group had treatment-related grade 3–4 adverse events: 24 (5%) in the atezolizumab plus bevacizumab group and 37 (8%) in the sunitinib group had treatment-related all-grade adverse events, which led to treatment-regimen discontinuation.

Interpretation: Atezolizumab plus bevacizumab prolonged progression-free survival versus sunitinib in patients with metastatic renal cell carcinoma and showed a favourable safety profile. Longer-term follow-up is necessary to establish whether a survival benefit will emerge. These study results support atezolizumab plus bevacizumab as a first-line treatment option for selected patients with advanced renal cell carcinoma.

Funding: F Hoffmann–La Roche Ltd and Genentech Inc.


Abstract:

Background: The level of evidence for HIV transmission risk through condomless sex in serodifferent gay couples with the HIV-positive partner taking virally suppressive antiretroviral therapy (ART) is limited compared with the evidence available for transmission risk in heterosexual couples. The aim of the second phase of the PARTNER study (PARTNER2) was to provide precise estimates of transmission risk in gay serodifferent partnerships.
Methods: The PARTNER study was a prospective observational study done at 75 sites in 14 European countries. The first phase of the study (PARTNER1; Sept 15, 2010, to May 31, 2014) recruited and followed up both heterosexual and gay serodifferent couples (HIV-positive partner taking suppressive ART) who reported condomless sex, whereas the PARTNER2 extension (to April 30, 2018) recruited and followed up gay couples only. At study visits, data collection included sexual behaviour questionnaires, HIV testing (HIV-negative partner), and HIV-1 viral load testing (HIV-positive partner). If a seroconversion occurred in the HIV-negative partner, anonymised phylogenetic analysis was done to compare HIV-1 \textit{pol} and \textit{env} sequences in both partners to identify linked transmissions. Couple-years of follow-up were eligible for inclusion if condomless sex was reported, use of pre-exposure prophylaxis or post-exposure prophylaxis was not reported by the HIV-negative partner, and the HIV-positive partner was virally suppressed (plasma HIV-1 RNA <200 copies per mL) at the most recent visit (within the past year). Incidence rate of HIV transmission was calculated as the number of phylogenetically linked HIV infections that occurred during eligible couple-years of follow-up divided by eligible couple-years of follow-up. Two-sided 95% CIs for the incidence rate of transmission were calculated using exact Poisson methods.

Findings: Between Sept 15, 2010, and July 31, 2017, 972 gay couples were enrolled, of which 782 provided 1593 eligible couple-years of follow-up with a median follow-up of 2·0 years (IQR 1·1–3·5). At baseline, median age for HIV-positive partners was 40 years (IQR 33–46) and couples reported condomless sex for a median of 1·0 years (IQR 0·4–2·9). During eligible couple-years of follow-up, couples reported condomless anal sex a total of 76 088 times. 288 (37%) of 777 HIV-negative men reported condomless sex with other partners. 15 new HIV infections occurred during eligible couple-years of follow-up, but none were phylogenetically linked within-couple transmissions, resulting in an HIV transmission rate of zero (upper 95% CI 0·23 per 100 couple-years of follow-up).

Interpretation: Our results provide a similar level of evidence on viral suppression and HIV transmission risk for gay men to that previously generated for heterosexual couples and suggest that the risk of HIV transmission in gay couples through condomless sex when HIV viral load is suppressed is effectively zero. Our findings support the message of the U=U (undetectable equals untransmittable) campaign, and the benefits of early testing and treatment for HIV.

Funding: National Institute for Health Research.
Abstract:

**Background:** Risk factors for maternal infection are clearly recognised, including caesarean section and operative vaginal birth. Antibiotic prophylaxis at caesarean section is widely recommended because there is clear systematic review evidence that it reduces incidence of maternal infection. Current WHO guidelines do not recommend routine antibiotic prophylaxis for women undergoing operative vaginal birth because of insufficient evidence of effectiveness. We aimed to investigate whether antibiotic prophylaxis prevented maternal infection after operative vaginal birth.

**Methods:** In a blinded, randomised controlled trial done at 27 UK obstetric units, women (aged ≥16 years) were allocated to receive a single dose of intravenous amoxicillin and clavulanic acid or placebo (saline) following operative vaginal birth at 36 weeks gestation or later. The primary outcome was confirmed or suspected maternal infection within 6 weeks of delivery defined by a new prescription of antibiotics for specific indications, confirmed systemic infection on culture, or endometritis. We did an intention-to-treat analysis. This trial is registered with ISRCTN, number 11166984, and is closed to accrual.

**Findings:** Between March 13, 2016, and June 13, 2018, 3427 women were randomly assigned to treatment: 1719 to amoxicillin and clavulanic acid, and 1708 to placebo. Seven women withdrew, leaving 1715 in the amoxicillin and clavulanic acid group and 1705 in the placebo groups. Primary outcome data were missing for 195 (6%) women. Significantly fewer women allocated to amoxicillin and clavulanic acid had a confirmed or suspected infection (180 [11%] of 1619) than women allocated to placebo (306 [19%] of 1606; risk ratio 0·58, 95% CI 0·49–0·69; p<0·0001). One woman in the placebo group reported a skin rash and two women in the amoxicillin and clavulanic acid reported other allergic reactions, one of which was reported as a serious adverse event. Two other serious adverse events were reported, neither was considered causally related to the treatment.
Interpretation: This trial shows benefit of a single dose of prophylactic antibiotic after operative vaginal birth and guidance from WHO and other national organisations should be changed to reflect this.

Funding: NIHR Health Technology Assessment programme.


Abstract:

Objectives: To evaluate the prevalence of special diet adoption in juvenile idiopathic arthritis (JIA) and parental perceptions of efficacy.

Design: An online survey was distributed over a year to nearly 20,000 individuals.

Results: Responses from 261 parents of patients with JIA were received. One of three \( n = 79 \) had tried special diets, including gluten-free (66%), anti-inflammatory (41%), and lactose-free (25%). Overall, >50% of 79 parents reported that patients had improved pain or joint swelling.

Conclusions: Special diets have been trialed by a third of the patients, with over half reporting symptom improvement. A prospective, controlled trial is warranted to test the efficacy of a dietary approach to JIA.


Abstract:

Despite global commitments to achieving gender equality and improving health and wellbeing for all, quantitative data and methods to precisely estimate the effect of gender norms on health inequities are underdeveloped. Nonetheless, existing global, national, and subnational data provide some key opportunities for testing associations between gender norms and health. Using innovative approaches to analysing proxies for gender norms, we generated evidence that gender norms impact the health of women and men across life stages, health sectors, and world regions. Six case studies showed that: (1) gender norms are complex and can intersect with other social factors to impact health over the life
course; (2) early gender-normative influences by parents and peers can have multiple and differing health consequences for girls and boys; (3) non-conformity with, and transgression of, gender norms can be harmful to health, particularly when they trigger negative sanctions; and (4) the impact of gender norms on health can be context-specific, demanding care when designing effective gender-transformative health policies and programmes. Limitations of survey-based data are described that resulted in missed opportunities for investigating certain populations and domains. Recommendations for optimising and advancing research on the health impacts of gender norms are made.


Abstract:

Background: Bortezomib, thalidomide, and dexamethasone (VTd) plus autologous stem-cell transplantation is standard treatment in Europe for transplant-eligible patients with newly diagnosed multiple myeloma. We evaluated whether the addition of daratumumab to VTd before and after autologous stem-cell transplantation would improve stringent complete response rate in patients with newly diagnosed multiple myeloma.
**Methods:** In this two-part, randomised, open-label, phase 3 CASSIOPEIA trial, we recruited transplant-eligible patients with newly diagnosed multiple myeloma at 111 European sites. Patients were randomly assigned (1:1) to receive four pre-transplant induction and two post-transplant consolidation cycles of VTd alone (VTd group) or in combination with daratumumab (D-VTd group). The primary endpoint of part 1 was stringent complete response assessed 100 days after transplantation. Part 2 (maintenance) is ongoing. The trial is registered with ClinicalTrials.gov, number NCT02541383.

**Findings:** Between Sept 22, 2015, and Aug 1, 2017, 1085 patients were enrolled at 111 European sites and were randomly assigned to the D-VTd group (n=543) or the VTd group (n=542). At day 100 after transplantation, 157 (29%) of 543 patients in the D-VTd group and 110 (20%) of 542 patients in the VTd group in the intention-to-treat population had achieved a stringent complete response (odds ratio 1·60, 95% CI 1·21–2·12, p=0·0010). 211 (39%) patients in the D-VTd group versus 141 (26%) in the VTd group achieved a complete response or better, and 346 (64%) of 543 versus 236 (44%) of 542 achieved minimal residual disease-negativity (10^-5 sensitivity threshold, assessed by multiparametric flow cytometry; both p<0·0001). Median progression-free survival from first randomisation was not reached in either group (hazard ratio 0·47, 95% CI 0·33–0·67, p<0·0001). 46 deaths on study were observed (14 vs 32, 0·43, 95% CI 0·23–0·80). The most common grade 3 or 4 adverse events were neutropenia (28% vs 15%), lymphopenia (17% vs 10%), and stomatitis (13% vs 16%).

**Interpretation:** D-VTd before and after autologous stem-cell transplantation improved depth of response and progression-free survival with acceptable safety. CASSIOPEIA is the first study showing the clinical benefit of daratumumab plus standard of care in transplant-eligible patients with newly diagnosed multiple myeloma.

**Funding:** The Intergroupe Francophone du Myélome and Dutch-Belgian Cooperative Trial Group for Hematology Oncology.

**Abstract:**
**Background:** Alcohol use is a leading risk factor for global disease burden, and data on alcohol exposure are crucial to evaluate progress in achieving global non-communicable disease goals. We present estimates on the main indicators of alcohol exposure for 189 countries from 1990–2017, with forecasts up to 2030.

**Methods:** Adult alcohol per-capita consumption (the consumption in L of pure alcohol per adult [≥15 years]) in a given year was based on country-validated data up to 2016. Forecasts up to 2030 were obtained from multivariate log-normal mixture Poisson distribution models. Using survey data from 149 countries, prevalence of lifetime abstinence and current drinking was obtained from Dirichlet regressions. The prevalence of heavy episodic drinking (30-day prevalence of at least one occasion of 60 g of pure alcohol intake among current drinkers) was estimated with fractional response regressions using survey data from 118 countries.

**Findings:** Between 1990 and 2017, global adult per-capita consumption increased from 5·9 L (95% CI 5·8–6·1) to 6·5 L (6·0–6·9), and is forecasted to reach 7·6 L (6·5–10·2) by 2030. Globally, the prevalence of lifetime abstinence decreased from 46% (42–49) in 1990 to 43% (40–46) in 2017, albeit this was not a significant reduction, while the prevalence of current drinking increased from 45% (41–48) in 1990 to 47% (44–50) in 2017. We forecast both trends to continue, with abstinence decreasing to 40% (37–44) by 2030 (annualised 0·2% decrease) and the proportion of current drinkers increasing to 50% (46–53) by 2030 (annualised 0·2% increase). In 2017, 20% (17–24) of adults were heavy episodic drinkers (compared with 1990 when it was estimated at 18·5% [15·3–21·6%]), and this prevalence is expected to increase to 23% (19–27) in 2030.

**Interpretation:** Based on these data, global goals for reducing the harmful use of alcohol are unlikely to be achieved, and known effective and cost-effective policy measures should be implemented to reduce alcohol exposure.

**Funding:** Centre for Addiction and Mental Health and the WHO Collaborating Center for Addiction and Mental Health at the Centre for Addiction and Mental Health.

Abstract:

**Background:** Guidelines recommend the use of nutritional support during hospital stays for medical patients (patients not critically ill and not undergoing surgical procedures) at risk of malnutrition. However, the supporting evidence for this recommendation is insufficient, and there is growing concern about the possible negative effects of nutritional therapy during acute illness on recovery and clinical outcomes. Our aim was thus to test the hypothesis that protocol-guided individualised nutritional support to reach protein and caloric goals reduces the risk of adverse clinical outcomes in medical inpatients at nutritional risk.

**Methods:** The Effect of early nutritional support on Frailty, Functional Outcomes, and Recovery of malnourished medical inpatients Trial (EFFORT) is a pragmatic, investigator-initiated, open-label, multicentre study. We recruited medical patients at nutritional risk (nutritional risk screening 2002 [NRS 2002] score ≥3 points) and with an expected length of hospital stay of more than 4 days from eight Swiss hospitals. These participants were randomly assigned (1:1) to receive either protocol-guided individualised nutritional support to reach protein and caloric goals (intervention group) or standard hospital food (control group). Randomisation was done with variable block sizes and stratification according to study site and severity of malnutrition using an interactive web-response system. In the intervention group, individualised nutritional support goals were defined by specialist dietitians and nutritional support was initiated no later than 48 h after admission. Patients in the control group received no dietary consultation. The composite primary endpoint was any adverse clinical outcome defined as all-cause mortality, admission to intensive care, non-elective hospital readmission, major complications, and decline in functional status at 30 days, and it was measured in all randomised patients who completed the trial. This trial is registered with ClinicalTrials.gov, number NCT02517476.
Findings: 5015 patients were screened, and 2088 were recruited and monitored between April 1, 2014, and Feb 28, 2018. 1050 patients were assigned to the intervention group and 1038 to the control group. 60 patients withdrew consent during the course of the trial (35 in the intervention group and 25 in the control group). During the hospital stay, caloric goals were reached in 800 (79%) and protein goals in 770 (76%) of 1015 patients in the intervention group. By 30 days, 232 (23%) patients in the intervention group experienced an adverse clinical outcome, compared with 272 (27%) of 1013 patients in the control group (adjusted odds ratio [OR] 0·79 [95% CI 0·64–0·97], p=0·023). By day 30, 73 [7%] patients had died in the intervention group compared with 100 [10%] patients in the control group (adjusted OR 0·65 [0·47–0·91], p=0·011). There was no difference in the proportion of patients who experienced side-effects from nutritional support between the intervention and the control group (162 [16%] vs 145 [14%], adjusted OR 1·16 [0·90–1·51], p=0·26).

Interpretation: In medical inpatients at nutritional risk, the use of individualised nutritional support during the hospital stay improved important clinical outcomes, including survival, compared with standard hospital food. These findings strongly support the concept of systematically screening medical inpatients on hospital admission regarding nutritional risk, independent of their medical condition, followed by a nutritional assessment and introduction of individualised nutritional support in patients at risk.

Funding: The Swiss National Science Foundation and the Research Council of the Kantonsspital Aarau, Switzerland.


Abstract:

Background: New-generation drug-eluting stents (DES) have mostly been investigated in head-to-head non-inferiority trials against early-generation DES and have typically shown similar efficacy and superior safety. How the safety profile of new-generation DES compares with that of bare-metal stents (BMS) is less clear.

Methods: We did an individual patient data meta-analysis of randomised clinical trials to compare outcomes after implantation of new-generation DES or BMS among patients undergoing percutaneous coronary intervention. The primary outcome was the composite of cardiac death or myocardial infarction. Data were pooled in a one-stage random-effects meta-analysis and examined at maximum follow-up and a 1-year landmark. Risk estimates are reported as hazard ratios (HRs) with 95% CIs. This study is registered in PROSPERO, number CRD42017060520.

Findings: We obtained individual data for 26,616 patients in 20 randomised trials. Mean follow-up was 3·2 (SD 1·8) years. The risk of the primary outcome was reduced in DES recipients compared with BMS recipients (HR 0·84, 95% CI 0·78–0·90, p<0·001) owing to a reduced risk of myocardial infarction (0·79, 0·71–0·88, p<0·001) and a possible slight but non-significant cardiac mortality benefit (0·89, 0·78–1·01, p=0·075). All-cause death was unaffected (HR with DES 0·96, 95% CI 0·88–1·05, p=0·358), but risk was lowered for definite stent thrombosis (0·63, 0·50–0·80, p<0·001) and target-vessel revascularisation (0·55, 0·50–0·60, p<0·001). We saw a time-dependent treatment effect, with DES being associated with lower risk of the primary outcome than BMS up to 1 year after placement. While the effect was maintained in the longer term, there was no further divergence from BMS after 1 year.

Interpretation: The performance of new-generation DES in the first year after implantation means that BMS should no longer be considered the gold standard for safety. Further development of DES technology should target improvements in clinical outcomes beyond 1 year.

Funding: Bern University Hospital.


**Abstract:**

**Background:** Glucagon-like peptide-1 (GLP-1) receptor agonists are effective treatments for type 2 diabetes, lowering glycated haemoglobin (HbA1c) and weight, but are currently only approved for use as subcutaneous injections. Oral semaglutide, a novel GLP-1 agonist, was compared with subcutaneous liraglutide and placebo in patients with type 2 diabetes.

**Methods:** In this randomised, double-blind, double-dummy, phase 3a trial, we recruited patients with type 2 diabetes from 100 sites in 12 countries. Eligible patients were aged 18 years or older, with HbA1c of 7·0–9·5% (53–80·3 mmol/mol), on a stable dose of metformin (≥1500 mg or maximum tolerated) with or without a sodium-glucose co-transporter-2 inhibitor. Participants were randomly assigned (2:2:1) with an interactive web-response system and stratified by background glucose-lowering medication and country of origin, to once-daily oral semaglutide (dose escalated to 14 mg), once-daily subcutaneous liraglutide (dose escalated to 1·8 mg), or placebo for 52 weeks. Two estimands were defined: treatment policy (regardless of study drug discontinuation or rescue medication) and trial product (assumed all participants were on study drug without rescue medication) in all participants who were randomly assigned. The treatment policy estimand was the primary estimand. The primary endpoint was change from baseline to week 26 in HbA1c (oral semaglutide superiority vs placebo and non-inferiority [margin: 0·4%] and superiority vs subcutaneous liraglutide) and the confirmatory secondary endpoint was change from baseline to week 26 in bodyweight (oral semaglutide superiority vs placebo and liraglutide). Safety was assessed in all participants who received at least one dose of study drug. This trial is registered on Clinicaltrials.gov, number NCT02863419, and the European Clinical Trials registry, number EudraCT 2015-005210-30.
**Findings:** Between Aug 10, 2016, and Feb 7, 2017, 950 patients were screened, of whom 711 were eligible and randomly assigned to oral semaglutide (n=285), subcutaneous liraglutide (n=284), or placebo (n=142). 341 (48%) of 711 participants were female and the mean age was 56 years (SD 10). All participants were given at least one dose of study drug, and 277 (97%) participants in the oral semaglutide group, 274 (96%) in the liraglutide group, and 134 (94%) in the placebo group completed the 52-week trial period. Mean change from baseline in HbA\textsubscript{1c} at week 26 was $-1.2\%$ (SE 0.1) with oral semaglutide, $-1.1\%$ (SE 0.1) with subcutaneous liraglutide, and $-0.2\%$ (SE 0.1) with placebo. Oral semaglutide was non-inferior to subcutaneous liraglutide in decreasing HbA\textsubscript{1c} (estimated treatment difference [ETD] $-0.1\%$, 95% CI $-0.3$ to $0.0$; $p<0.0001$) and superior to placebo (ETD $-1.1\%$, $-1.2$ to $-0.9$; $p<0.0001$) by use of the treatment policy estimand. By use of the trial product estimand, oral semaglutide had significantly greater decreases in HbA\textsubscript{1c} than both subcutaneous liraglutide (ETD $-0.2\%$, 95% CI $-0.3$ to $-0.1$; $p=0.0056$) and placebo (ETD $-1.2\%$, $-1.4$ to $-1.0$; $p<0.0001$) at week 26. Oral semaglutide resulted in superior weight loss ($-4.4$ kg [SE 0.2]) compared with liraglutide ($-3.1$ kg [SE 0.2]; ETD $-1.2$ kg, 95% CI $-1.9$ to $-0.6$; $p=0.0003$) and placebo ($-0.5$ kg [SE 0.3]; ETD $-3.8$ kg, $-4.7$ to $-3.0$; $p<0.0001$) at week 26 (treatment policy). By use of the trial product estimand, weight loss at week 26 was significantly greater with oral semaglutide than with subcutaneous liraglutide ($-1.5$ kg, 95% CI $-2.2$ to $-0.9$; $p<0.0001$) and placebo (ETD $-4.0$ kg, $-4.8$ to $-3.2$; $p<0.0001$). Adverse events were more frequent with oral semaglutide (n=229 [80%]) and subcutaneous liraglutide (n=211 [74%]) than with placebo (n=95 [67%]).

**Interpretation:** Oral semaglutide was non-inferior to subcutaneous liraglutide and superior to placebo in decreasing HbA\textsubscript{1c}, and superior in decreasing bodyweight compared with both liraglutide and placebo at week 26. Safety and tolerability of oral semaglutide were similar to subcutaneous liraglutide. Use of oral semaglutide could potentially lead to earlier initiation of GLP-1 receptor agonist therapy in the diabetes treatment continuum of care.

**Funding:** Novo Nordisk A/S.

Recognising physicians with impairment. Lancet 2019; 393(10189): 2360

Refugee health is a crisis of our own making. Lancet 2019; 393(10191): 2563p.


Abstract:

**Background:** Loss of arm function is a common problem after stroke. Robot-assisted training might improve arm function and activities of daily living. We compared the clinical effectiveness of robot-assisted training using the MIT-Manus robotic gym with an enhanced upper limb therapy (EULT) programme based on repetitive functional task practice and with usual care.

**Methods:** RATULS was a pragmatic, multicentre, randomised controlled trial done at four UK centres. Stroke patients aged at least 18 years with moderate or severe upper limb functional limitation, between 1 week and 5 years after their first stroke, were randomly assigned (1:1:1) to receive robot-assisted training, EULT, or usual care. Robot-assisted training and EULT were provided for 45 min, three times per week for 12 weeks. Randomisation was internet-based using permuted block sequences. Treatment allocation was masked from outcome assessors but not from participants or therapists. The primary outcome was upper limb function success (defined using the Action Research Arm Test [ARAT]) at 3 months. Analyses were done on an intention-to-treat basis. This study is registered with the ISRCTN registry, number ISRCTN69371850.
**Findings:** Between April 14, 2014, and April 30, 2018, 770 participants were enrolled and randomly assigned to either robot-assisted training (n=257), EULT (n=259), or usual care (n=254). The primary outcome of ARAT success was achieved by 103 (44%) of 232 patients in the robot-assisted training group, 118 (50%) of 234 in the EULT group, and 85 (42%) of 203 in the usual care group. Compared with usual care, robot-assisted training (adjusted odds ratio [aOR] 1·17 [98·3% CI 0·70–1·96]) and EULT (aOR 1·51 [0·90–2·51]) did not improve upper limb function; the effects of robot-assisted training did not differ from EULT (aOR 0·78 [0·48–1·27]). More participants in the robot-assisted training group (39 [15%] of 257) and EULT group (33 [13%] of 259) had serious adverse events than in the usual care group (20 [8%] of 254), but none were attributable to the intervention.

**Interpretation:** Robot-assisted training and EULT did not improve upper limb function after stroke compared with usual care for patients with moderate or severe upper limb functional limitation. These results do not support the use of robot-assisted training as provided in this trial in routine clinical practice.

**Funding:** National Institute for Health Research Health Technology Assessment Programme.


**Abstract:**

**Background:** Gonorrhoea is a common sexually transmitted infection for which ceftriaxone is the current first-line treatment, but antimicrobial resistance is emerging. The objective of this study was to assess the effectiveness of gentamicin as an alternative to ceftriaxone (both combined with azithromycin) for treatment of gonorrhoea.
**Methods:** G-ToG was a multicentre, parallel-group, pragmatic, randomised, non-inferiority trial comparing treatment with gentamicin to treatment with ceftriaxone for patients with gonorrhoea. The patients, treating physician, and assessing physician were masked to treatment but the treating nurse was not. The trial took place at 14 sexual health clinics in England. Adults aged 16–70 years were eligible for participation if they had a diagnosis of uncomplicated genital, pharyngeal, or rectal gonorrhoea. Participants were randomly assigned to receive a single intramuscular dose of either gentamicin 240 mg (gentamicin group) or ceftriaxone 500 mg (ceftriaxone group). All participants also received a single 1 g dose of oral azithromycin. Randomisation (1:1) was stratified by clinic and performed using a secure web-based system. The primary outcome was clearance of *Neisseria gonorrhoeae* at all initially infected sites, defined as a negative nucleic acid amplification test 2 weeks post treatment. Primary outcome analyses included only participants who had follow-up data, irrespective of the baseline visit *N gonorrhoeae* test result. The margin used to establish non-inferiority was a lower confidence limit of 5% for the risk difference. This trial is registered with ISRCTN, number ISRCTN51783227.

**Findings:** Of 1762 patients assessed, we enrolled 720 participants between Oct 7, 2014, and Nov 14, 2016, and randomly assigned 358 to gentamicin and 362 to ceftriaxone. Primary outcome data were available for 306 (85%) of 362 participants allocated to ceftriaxone and 292 (82%) of 358 participants allocated to gentamicin. At 2 weeks after treatment, infection had cleared for 299 (98%) of 306 participants in the ceftriaxone group compared with 267 (91%) of 292 participants in the gentamicin group (adjusted risk difference −6·4%, 95% CI −10·4% to −2·4%). Of the 328 participants who had a genital infection, 151 (98%) of 154 in the ceftriaxone group and 163 (94%) of 174 in the gentamicin group had clearance at follow-up (adjusted risk difference −4·4%, −8·7 to 0). For participants with a pharyngeal infection, a greater proportion receiving ceftriaxone had clearance at follow-up (108 [96%] in the ceftriaxone group compared with 82 [80%] in the gentamicin group; adjusted risk difference −15·3%, −24·0 to −6·5). Similarly, a greater proportion of participants with rectal infection in the ceftriaxone group had clearance (134 [98%] in the ceftriaxone group compared with 107 [90%] in the gentamicin group; adjusted risk difference −7·8%, −13·6 to −2·0). Thus, we did not find that a single dose of gentamicin 240 mg was non-inferior to a single dose of ceftriaxone 500 mg for the treatment of gonorrhoea, when both drugs were combined with a 1 g dose of oral azithromycin. The side-effect profiles were similar between groups, although severity of pain at the injection site was higher for gentamicin (mean visual analogue pain score 36 of 100 in the gentamicin group vs 21 of 100 in the ceftriaxone group).
**Interpretation:** Gentamicin is not appropriate as first-line treatment for gonorrhoea but remains potentially useful for patients with isolated genital infection, or for patients who are allergic or intolerant to ceftriaxone, or harbour a ceftriaxone-resistant isolate. Further research is required to identify and test new alternatives to ceftriaxone for the treatment of gonorrhoea.

**Funding:** UK National Institute for Health Research.


**Abstract:**

**Background:** Antiplatelet therapy reduces the risk of major vascular events for people with occlusive vascular disease, although it might increase the risk of intracranial haemorrhage. Patients surviving the commonest subtype of intracranial haemorrhage, intracerebral haemorrhage, are at risk of both haemorrhagic and occlusive vascular events, but whether antiplatelet therapy can be used safely is unclear. We aimed to estimate the relative and absolute effects of antiplatelet therapy on recurrent intracerebral haemorrhage and whether this risk might exceed any reduction of occlusive vascular events.

**Methods:** The REstart or STop Antithrombotics Randomised Trial (RESTART) was a prospective, randomised, open-label, blinded endpoint, parallel-group trial at 122 hospitals in the UK. We recruited adults (≥18 years) who were taking antithrombotic (antiplatelet or anticoagulant) therapy for the prevention of occlusive vascular disease when they developed intracerebral haemorrhage, discontinued antithrombotic therapy, and survived for 24 h. Computerised randomisation incorporating minimisation allocated participants (1:1) to start or avoid antiplatelet therapy. We followed participants for the primary outcome (recurrent symptomatic intracerebral haemorrhage) for up to 5 years. We analysed data from all randomised participants using Cox proportional hazards regression, adjusted for minimisation covariates. This trial is registered with ISRCTN (number ISRCTN71907627).
**Findings:** Between May 22, 2013, and May 31, 2018, 537 participants were recruited a median of 76 days (IQR 29–146) after intracerebral haemorrhage onset: 268 were assigned to start and 269 (one withdrew) to avoid antiplatelet therapy. Participants were followed for a median of 2·0 years (IQR [1·0– 3·0]; completeness 99·3%). 12 (4%) of 268 participants allocated to antiplatelet therapy had recurrence of intracerebral haemorrhage compared with 23 (9%) of 268 participants allocated to avoid antiplatelet therapy (adjusted hazard ratio 0·51 [95% CI 0·25–1·03]; p=0·060). 18 (7%) participants allocated to antiplatelet therapy experienced major haemorrhagic events compared with 25 (9%) participants allocated to avoid antiplatelet therapy (0·71 [0·39–1·30]; p=0·27), and 39 (15%) participants allocated to antiplatelet therapy had major occlusive vascular events compared with 38 (14%) allocated to avoid antiplatelet therapy (1·02 [0·65–1·60]; p=0·92).

**Interpretation:** These results exclude all but a very modest increase in the risk of recurrent intracerebral haemorrhage with antiplatelet therapy for patients on antithrombotic therapy for the prevention of occlusive vascular disease when they developed intracerebral haemorrhage. The risk of recurrent intracerebral haemorrhage is probably too small to exceed the established benefits of antiplatelet therapy for secondary prevention.

**Funding:** British Heart Foundation.

Abstract:

Background: Upadacitinib, an oral Janus kinase (JAK)1-selective inhibitor, showed efficacy in combination with stable background conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) in patients with rheumatoid arthritis who had an inadequate response to DMARDS. We aimed to evaluate the safety and efficacy of upadacitinib monotherapy after switching from methotrexate versus continuing methotrexate in patients with inadequate response to methotrexate.

Methods: SELECT-MONOTHERAPY was conducted at 138 sites in 24 countries. The study enrolled adults (≥18 years) who fulfilled the 2010 American College of Rheumatology (ACR)–European League Against Rheumatism (EULAR) classification criteria for rheumatoid arthritis. Patients with active rheumatoid arthritis despite stable methotrexate were randomly assigned 2:2:1:1 to switch to once-daily monotherapy of upadacitinib 15 mg or 30 mg or to continue methotrexate at their existing dose as blinded study drug; starting from week 14, patients assigned to continue methotrexate were switched to 15 mg or 30 mg once-daily upadacitinib per prespecified random assignment at baseline. The primary endpoints in this report are proportion of patients achieving 20% improvement in the ACR criteria (ACR20) at week 14, and proportion achieving low disease activity defined as 28-joint Disease Activity Score using C-reactive protein (DAS28[CRP]) of 3·2 or lower, both with non-responder imputation at week 14. Outcomes were assessed in patients who received at least one dose of study drug. This study is active but not recruiting and is registered with ClinicalTrials.gov, number NCT02706951.

Findings: Patients were screened between Feb 23, 2016, and May 19, 2017 and 648 were randomly assigned to treatment. 598 (92%) completed week 14. At week 14, an ACR20 response was achieved by 89 (41%) of 216 patients (95% CI 35–48) in the continued methotrexate group, 147 (68%) of 217 patients (62–74) receiving upadacitinib 15 mg, and 153 (71%) of 215 patients (65–77) receiving upadacitinib 30 mg (p<0·0001 for both doses vs continued methotrexate). DAS28(CRP) 3·2 or lower was met by 42 (19%) of 216 (95% CI 14–25) in the continued methotrexate group, 97 (45%) of 217 (38–51) receiving upadacitinib 15 mg, and 114 (53%) of 215 (46–60) receiving upadacitinib 30 mg (p<0·0001
for both doses vs continued methotrexate). Adverse events were reported in 102 patients (47%) on continued methotrexate, 103 (47%) on upadacitinib 15 mg, and 105 (49%) on upadacitinib 30 mg. Herpes zoster was reported by one (<1%) patient on continued methotrexate, three (1%) on upadacitinib 15 mg, and six (3%) on upadacitinib 30 mg. Three malignancies (one [<1%] on continued methotrexate, two [1%] on upadacitinib 15 mg), three adjudicated major adverse cardiovascular events (one [<1%] on upadacitinib 15 mg, two [<1%] on upadacitinib 30 mg), one adjudicated pulmonary embolism (<1%; upadacitinib 15 mg), and one death (<1%; upadacitinib 15 mg, haemorrhagic stroke [ruptured aneurysm]) were reported in the study.

**Interpretation:** Upadacitinib monotherapy showed statistically significant improvements in clinical and functional outcomes versus continuing methotrexate in this methotrexate inadequate-responder population. Safety observations were similar to those in previous upadacitinib rheumatoid arthritis studies.

**Funding:** AbbVie Inc, USA.


**Abstract:**

**Background:** Intradermal administration of fractional inactivated poliovirus vaccine (fIPV) is a dose-sparing alternative to the intramuscular full dose. We aimed to compare the immunogenicity of two fIPV doses versus one IPV dose for routine immunisation, and also assessed the immunogenicity of an fIPV booster dose for an outbreak response.

**Methods:** We did an open-label, randomised, controlled, inequality, non-inferiority trial in two clinics in Dhaka, Bangladesh. Healthy infants were randomly assigned at 6 weeks to one of four groups: group A received IPV at age 14 weeks and IPV booster at age 22 weeks; group B received IPV at age 14 weeks and fIPV booster at age 22 weeks; group C received IPV at age 6 weeks and fIPV booster at age 22 weeks; and group D received fIPV at 6 weeks and 14 weeks and fIPV booster at age 22 weeks. IPV was administered by needle-syringe as an intramuscular full dose (0·5 mL), and fIPV was administered intradermally (0·1 mL of the IPV formulation was administered using the 0·1 mL HelmJect auto-disable syringe with a Helms intradermal adapter). Both IPV and fIPV were administered on the outer, upper right thigh of infants. The primary outcome was vaccine
response to poliovirus types 1, 2, and 3 at age 22 weeks (routine immunisation) and age 26 weeks (outbreak response). Vaccine response was defined as seroconversion from seronegative (<1:8) at baseline to seropositive (≥1:8) or four-fold increase in reciprocal antibody titres adjusted for maternal antibody decay and was assessed in the modified intention-to-treat population (infants who received polio vaccines per group assignment and polio antibody titre results to serotypes 1, 2, and 3 at 6, 22, 23, and 26 weeks of age). The non-inferiority margin was 12·5%. This trial is registered with ClinicalTrials.gov, number NCT02847026.

**Findings:** Between Sept 1, 2016 and May 2, 2017, 1076 participants were randomly assigned and included in the modified intention-to-treat analysis: 271 in Group A, 267 in group B, 268 in group C, and 270 in group D. Vaccine response at 22 weeks to two doses of fIPV (group D) was significantly higher (p<0·0001) than to one dose of IPV (groups A and B) for all three poliovirus serotypes: the type 1 response comprised 212 (79% [95% CI 73–83]) versus 305 (57% [53–61]) participants, the type 2 response comprised 173 (64% [58–70]) versus 249 (46% [42–51]) participants, and the type 3 response comprised 196 (73% [67–78]) versus 196 (36% [33–41]) participants. At 26 weeks, the fIPV booster was non-inferior to IPV (group B vs group A) for serotype 1 (−1·12% [90% CI −2·18 to −0·06]), serotype 2 (0·40%, [−2·22 to 1·42]), and serotype 3 (1·51% [−3·23 to −0·21]). Of 129 adverse events, 21 were classified as serious including one death; none were attributed to IPV or fIPV.

**Interpretation:** fIPV appears to be an effective dose-sparing strategy for routine immunisation and outbreak responses.

**Funding:** US Centers for Disease Control and Prevention.


Abstract:
**Introduction:** Vascular aging is an independent risk factor for cardiovascular diseases, which has always been a research hotspot. This study aims to establish a Multiple Linear Regression (MLR) model using radial artery pulse wave characteristic parameters to assess vascular aging.

**Methods:** Data from 111 males and 117 females were used to propose a new method for extracting pulse wave characteristic parameters called, Equal Pressure Pulse Transit Time (EP-PTT). Firstly, 10 EP-PTTs were extracted from pulse waves which were used to describe the shape characteristics of the pulse signal. Secondly, 10 EP-PTTs were fed into MLR model, which were used to optimize the model. Lastly, the predicted age of all subjects was calculated by the optimal model. We compared the correlation coefficients of predicted age with Pulse Transit Time (PTT) and Augmentation Index (AIx) with the correlation coefficients of chronological age with PTT and AIx.

**Results:** 9 EP-PTTs were relevant to predicting age in men and all EP-PTTs were age-related in women (*P*<0.05). MLR analysis showed that EP-PTT<sub>3</sub> and EP-PTT<sub>7</sub> were potent predictors of vascular age in men but EP-PTT<sub>4</sub> and EP-PTT<sub>7</sub> were important predictors in women (*P*<0.001). Comparing with the chronological age, the predicted age was closer to PTT (*P*<0.001, *r*=-0.53 to *P*<0.001, *r*=-0.59 in men; *P*<0.001, *r*=-0.57 to *P*<0.001, *r*=-0.65 in women) and AIx (*P*<0.001, *r*=0.64 to *P*<0.001, *r*=0.81 in men; *P*<0.001, *r*=0.51 to *P*<0.001, *r*=0.56 in women).

**Conclusions:** The predicted age can better reflect vascular aging than chronological age. This proved the validity of the proposed method for assessing vascular aging.


