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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)
Junior Librarian
AYUSH & Other Systems


Abstract:

Background: We aimed to investigate why medical students in Germany participate in elective courses on acupuncture or homeopathy.

Methods: The study was a nationwide, cross-sectional survey. Elective courses on acupuncture and homeopathy in the academic half-year 2013/14 were identified by inquiries directed to all 37 German medical schools, to student initiatives, and organizations supporting such courses. Participants of courses were asked to fill in a questionnaire consisting of a free-text question on their motives and closed questions regarding personal experiences, personal environment, evidence, role of the therapy as a complement to conventional medicine, and opportunistic aspects in relation to the therapy chosen.

Results: Students participating in 16 of 18 identified acupuncture courses (n = 220) and 12 of 13 identified homeopathy courses (n = 113) filled in the questionnaire. Content analysis of the free text showed that personal experience, a feeling that conventional medicine is somehow incomplete, the belief that acupuncture or homeopathy could help to overcome this shortcoming, and positive characteristics attributed to the therapies were the main motives for participation. Quantitative analyses showed that own experiences and considering the therapy a useful complement to conventional medicine were similarly rated motives in both groups, while opportunistic aspects played almost no role. The influence of the personal environment was more important among homeopathy students, while acupuncture students considered their therapy better backed by evidence.

Conclusion: In our survey, personal experiences and the belief that acupuncture or homeopathy allows grasping the patient more holistically were primary motives for participation.


Abstract:

Introduction: This review explores the benefit/risk balance of using subcutaneous injections. Overall, regulatory authorities regard that the use of injectables are only justified for acute cases and that oral products are better alternatives for both ethical and safety reasons. Conversely, Complementary & Alternative Medicine (CAM) pharmaceutical companies and doctors who prescribe injectables consider them to have additional clinical value compared with the oral route of administration (ROA), and consider the risk of the parenteral ROA as very low.

Methods: A narrative review was conducted. The favourable and unfavourable effects, the uncertainty of the effects and the possible mode of action of the subcutaneous ROA are described and an estimation of the benefit/risk balance is performed.
**Results:** The review demonstrates a high prescribers demand, and evidence on the existence of several favourable effects of the subcutaneous ROA (e.g., higher clinical efficacy, higher bio-availability, quicker onset of action), some unfavourable low risk effects of the subcutaneous ROA (e.g., risk related to exposure, substance and the needle) and overall a positive benefit/risk balance.

**Conclusion:** The results justify a more positive attitude from regulatory authorities towards the use of this ROA and towards ampoule prescribing doctors. However, given the small number of good studies on this topic, more research on the favourable and unfavourable effects, the uncertainties of these effects and the conceptualization of the working mechanism of the subcutaneous ROA is indicated.


**Bazarganipour Fatemeh, Taghavi Seyed Abdolvahab, Allan Helen et al. Randomized controlled clinical trial evaluating quality of life when using a simple acupressure protocol in women with primary dysmenorrhea. Complementary Therapies in Medicine 2017; 34: 10-15p.**

**Abstract:**

**Objective:** To evaluate a simple acupressure protocol in LIV3 and LI4 acupoints in women with primary dysmenorrhea.

**Methods:** This paper reports a randomized, single blinded clinical trial. 90 young women with dysmenorrhea were recruited to three groups to receive 20 min acupressure every day in either LIV3 or LI4, or placebo points. Acupressure was timed five days before menstruation for three successive menstrual cycles. On menstruation, each participant completed the Wong Baker faces pain scale, and the quality of life short form −12 (QOL SF-12).

**Results:** Intensity and duration of pain between the three groups in the second and third cycles during the intervention (p < 0.05) differed significantly. Significant differences were seen in all domains of QOL except for mental health (p = 0.4), general health (p = 0.7) and mental subscale component (p = 0.12) in the second cycle, and mental health (p = 0.9), and mental subscale component (p = 0.14) in the third cycle.

**Conclusion:** Performing the simple acupressure protocol is an effective method to decrease the intensity and duration of dysmenorrhea, and improve the QOL.

**Canaway Rachel. Integration of traditional and ‘modern’ medicine: Reflections on a visit to DPR Korea. European Journal of Integrative Medicine 2017; 15: 32-38p.**


**Abstract:**

Nanoparticulate forms of metallic copper, commonly used as Cuprum metallicum in homeopathic medical practice, have shown promise as a potential antimicrobial agent for assisting in wound healing. Montmorillonite (MMT) clays have excellent adsorptive
capacity and may function as an excellent vehicle to increase the bioavailability of the nanoparticles of copper.

The study compared the current standard therapy (topical soframycin) for superficial wounds to Curprum metalliccum in three different attenuations adsorbed in MMT clay for the treatment of artificially induced wounds in mouse subjects. Field Emission Scanning Electron Microscopy was used to evaluate the nanoparticle adsorption in MMT clay for each of these attenuations. Outcomes were measured for cell regeneration of degeneration on histological examination after 28 days of treatment. The mice treated with all three attenuations of Cuprum metallicum in MMT and standard therapy soframycin demonstrated significantly better outcomes in both measures compared to control subjects. Treatment with the highest attenuation of Cuprum metallicum (200C) in MMT was not statistically different from the standard treatment, Soframycin, in the regenerated cells outcome measure. Cuprum metallicum in MMT shows promise for an alternate, safe, inexpensive, and effective therapy for superficial wounds.


Abstract:

Objectives: This study’s aims are to examine the effects of aromatherapy massage on women’s stress and immune function during pregnancy.

Methods: This longitudinal, prospective, randomized controlled trial recruited 52 healthy pregnant women from a prenatal clinic in Taipei using convenience sampling. The participants were randomly assigned to the intervention (n = 24) or control (n = 28) group using Clinstat block randomization. The intervention group received 70 min of aromatherapy massage with 2% lavender essential oil every other week (10 times in total) for 20 weeks; the control group received only routine prenatal care. In both groups, participants’ salivary cortisol and immunoglobulin A (IgA) levels were collected before and after the intervention group received aromatherapy massage (every month from 16 to 36 weeks gestation) and were analyzed using enzyme-linked immunosorbent assay.

Results: The pregnant women in the intervention group had lower salivary cortisol (p < 0.001) and higher IgA (p < 0.001) levels immediately after aromatherapy massage than those in the control group, which did not receive massage treatment. Comparing the long-term effects of aromatherapy massage on salivary IgA levels between groups at different times, the study found that the pretest salivary IgA levels at 32 (p = 0.002) and 36 (p < 0.001) weeks gestational age (GA) were significantly higher than the pretest IgA at 16 weeks GA (baseline).

Conclusions: This study presented evidence that aromatherapy massage could significantly decrease stress and enhance immune function in pregnant women. The findings can guide clinicians or midwives in providing aromatherapy massage to women throughout the pregnancy.


Abstract:

Objectives: To investigate the prevalence of complementary and alternative medicine (CAM) use, including botanical/herbal remedies, among Hispanic and non-Hispanic white women from the Study of Women's Health Across the Nation (SWAN), New Jersey site. We also examined whether attitudes toward CAM and communication of its use to providers differed for Hispanic and non-Hispanic women.

Study design: SWAN is a community-based, multiethnic cohort study of midlife women. At the 13th SWAN follow-up, women at the New Jersey site completed both a general CAM questionnaire and a culturally sensitive CAM questionnaire designed to capture herbal products commonly used in Hispanic/Latina communities. Prevalence of and attitudes toward CAM use were compared by race/ethnicity and demographic characteristics.

Results: Among 171 women (average age 61.8 years), the overall prevalence of herbal remedy use was high in both Hispanic and non-Hispanic white women (88.8% Hispanic and 81.3% non-Hispanic white), and prayer and herbal teas were the most common modalities used. Women reported the use of multiple herbal modalities (mean 6.6 for Hispanic and 4.0 for non-Hispanic white women; p = 0.001). Hispanic women were less likely to consider herbal treatment drugs (16% vs. 37.5%; p = 0.005) and were less likely to report sharing the use of herbal remedies with their doctors (14.4% Hispanic vs. 34% non-Hispanic white; p = 0.001). The number of modalities used was similar regardless of the number of prescription medications used.

Conclusions: High prevalence of herbal CAM use was observed for both Hispanic and non-Hispanic white women. Results highlight the need for healthcare providers to query women regarding CAM use to identify potential interactions with traditional treatments and to determine whether CAM is used in lieu of traditional medications.


Abstract:

Background and aims: Colonoscopy can be painful and uncomfortable. Aromatherapy is often used for the relief of anxiety or discomfort. Recently, it has been reported that olfactory stimulation induces various physiological effects. We investigated the effects of aromatherapy on anxiety and abdominal discomfort during colonoscopy.

Methods: The investigation was carried out using a randomized controlled study. Aromatherapy was performed by vapor diffusion, and each patient was given one of the
following treatments: no inhalation (control group), essential-oil-less vapor (vehicle group), lavender oil (lavender group), grapefruit oil (grapefruit group), or Osmanthus fragrans oil (Osmanthus fragrans group). Following total colonoscopy procedures, each patient estimated their anxiety and abdominal discomfort using the Numeric Rating Scale.

**Results:** Total colonoscopy was performed on 361 patients. No complications caused by colonoscopy or aromatherapy were experienced. In the Osmanthus fragrans group, anxiety was significantly attenuated. The abdominal discomfort of patients who reported strong anxiety during colonoscopy was significantly attenuated in the grapefruit group and the Osmanthus fragrans group.

**Conclusion:** Aromatherapies using Osmanthus fragrans oil and grapefruit oil are effective complementary treatments for anxious patients undergoing colonoscopy.


**Abstract:**

**Objectives:** The present study aimed to compare the effects of music and music video interventions on objective and subjective sleep quality in adults with sleep disturbances.

**Design:** A randomized controlled trial was performed on 71 adults who were recruited from the outpatient department of a hospital with 1100 beds and randomly assigned to the control, music, and music video groups.

**Interventions:** During the 4 test days (Days 2–5), for 30 min before nocturnal sleep, the music group listened to Buddhist music and the music video group watched Buddhist music videos. They were instructed to not listen/watch to the music/MV on the first night (pretest, Day 1) and the final night (Day 6). The control group received no intervention.

**Main outcome measures:** Sleep was assessed using a one-channel electroencephalography machine in their homes and self-reported questionnaires.

**Results:** The music and music video interventions had no effect on any objective sleep parameters, as measured using electroencephalography. However, the music group had significantly longer subjective total sleep time than the music video group did (Wald $\chi^2 = 6.23$, $p = 0.04$).

**Conclusion:** Our study results increase knowledge regarding music interventions for sleep quality in adults with sleep disturbances. This study suggested that more research is required to strengthen the scientific knowledge of the effects of music intervention on sleep quality in adults with sleep disturbances. (ISRCTN94971645)


Abstract:

Objectives: This study aims to investigate the effects of meridian acupressure massage on body composition, edema, stress, and fatigue in postpartum women.

Design: A quasi-experimental design with a nonequivalent control group was utilized.

Settings/Location: The Postpartum Care Center of Women’s Hospital in Gwangju City, Republic of Korea.

Subjects: The study group consisted of 39 postpartum women, 19 in the experimental group and 20 in the control group, recruited from the postpartum care center of Women’s Hospital in Gwangju city, South Korea.

Interventions: The experimental group was provided with meridian acupressure massage for 90 min daily over 5 days as an experimental therapy.

Outcome measures: Body composition (body weight, BMI, total body water, ECW ratio, LBM, and body fat) Edema (subjective edema, average girth of the upper limbs, and average girth of the lower limbs), Stress (psychological stress and physical stress), and Fatigue.

Results: The experimental group demonstrated a significantly larger decrease compared with the control group in measures of body composition, edema, total subjective stress, psychological stress, and subjective fatigue.

Conclusions: Meridian acupressure massage can hasten the return to original body composition after childbirth.


Abstract:

Objectives: Ayurveda claims to be effective in the treatment of psychosomatic disorders by means of lifestyle and nutritional counseling.

Design: In a randomized controlled study mothers with burnout were randomized into two groups: Ayurvedic nutritional counseling (according to tradition), and conventional nutritional counseling (following the recommendations of a family doctor). Patients received five counseling sessions over twelve weeks.

Main outcome measures: Outcomes included levels of burnout, quality of life, sleep, stress, depression/anxiety, and spirituality at three and six months. It also included a qualitative evaluation of the communication processes.

Results: We randomized thirty four patients; twenty three participants were included in the per protocol analysis. No significant differences were observed between the groups. However, significant and clinically relevant intra-group mean changes for the primary outcome burnout, and secondary outcomes sleep, stress, depression and mental health were only found in the Ayurveda group. The qualitative part of the study identified different conversational styles and counseling techniques between the two
study groups. In conventional consultations questions tended to be category bound, while counseling-advice was predominantly admonitory. The Ayurvedic practitioner used open-ended interrogative forms, devices for displaying understanding, and positive re-evaluation more frequently, leading to an overall less asymmetrical interaction.

**Conclusions:** We found positive effects for both groups, which however were more pronounced in the Ayurvedic group. The conversational and counseling techniques in the Ayurvedic group offered more opportunities for problem description by patients as well as patient-centered practice and resource-oriented recommendations by the physician.


**Abstract:**

**Introduction:** Pattern identification (PI) is a unique concept in traditional East Asian medicine that refers to diagnostic process. This study aims to summarize and critically evaluate the reliability and validity of all Korean designed PI instruments.

**Methods:** A systematic literature search was conducted in MEDLINE, EMBASE, and eight Korean medical databases from the study's inception to August 2017 to identify all studies that described Korean PI instruments. We included PI instruments without restriction on the types of diseases or, conditions of participants. General characteristics of the included instruments, reliability verification, internal consistency, and the types of validity, including construct validity, content validity, and criterion validity, were reviewed.

**Results:** Thirty-six PI instruments were identified and analyzed. Ten of them were PI diagnostic tools for specific diseases. Fifteen were related diagnoses of PI for non-specific diseases. Four instruments involved the diagnosis of PI for specific decoction treatment and seven were related to the diagnosis of constitution, including Sasang constitution. The most commonly used statistical test was Cronbach’s alpha, an estimator of internal consistency. A total of ten studies conducted test-retest reliability with varying time intervals, and the test-retest coefficient was moderate to good.

**Conclusions:** This article examined the reliability and validity of the PI instruments used in Korea and the need to improve the standardisation of PI diagnosis. Almost studies reported the value of internal consistency only. Clinical studies on the application of future questionnaires will be needed in the future.


**Abstract:**

**Introduction:** Evidence-based medicine (EBM) has become an important part of medical education. Students’ perception and demand are important in education. The
Aim of our study was to conduct a nationwide online survey about EBM in traditional Korean Medicine (KM) education.

**Methods:** An online questionnaire was developed, comprising categories about EBM education in KM. Student’s experience, achievement, satisfaction, understanding and expectation in EBM education were surveyed. Face validity of the developed questionnaire was tested before survey and online links were sent through SurveyMonkey to all KM college students in Korea.

**Results:** Among the total 4649 students nationwide, 1292 agreed to participate in the survey (response rate: 27.8%) within 10 days. Self-appraisals about the achievement, satisfaction, and understanding of EBM were relatively low. In addition to this, 30% of students answered they did not learn about EBM in regular school curriculum. Expectation of extension of further EBM education curriculum was comparatively high. Most respondents agreed that EBM knowledge would be useful for clinical practice and the undergraduate curriculum. Barriers to enhance EBM education were perceived to be lack of resources and appropriate contents.

**Conclusion:** This first nationwide survey in Korea investigated the experience, perception, and demand for EBM education by KM college students. The importance of EBM education in the KM curriculum needs further improvement and curriculum development based on the students’ experiences and perceptions. Additionally, online survey in smartphone environment, which was conducted thorough involvement of student’s representatives seems to be an eligible strategy for a survey of students.


**Abstract:**

Homeopathy is often overlooked as a modality for pain management. However, it deserves to be a first-line treatment due to its safety, effectiveness, and cost-effectiveness. Limitations to the acceptance of homeopathy in the United States include physicians’ lack of familiarity with the research studies, which primarily come from Europe, where homeopathy is integrated into the national healthcare systems of nearly all European countries. The database of the social security system in France, where citizens can choose a homeopathic or conventional family doctor, shows that the former modality provides comparable results in pain management while significantly reducing the use of conventional painkillers. Research in the United States is minimal due to lack of government or industry funding. In addition, exaggerated media reports as to the potential harm from homeopathy have resulted in undue reluctance to use it among both physicians and the general public. A large-scale review of the German drug safety database has revealed a miniscule number of adverse events. Finally, resistance to the use of homeopathy—based on the mistaken notion that it contains nothing but water—is addressed by citations from the newly emerging field of ultrahigh dilution physics. A description of the most common homeopathic medicines for various types of pain is provided, including back pain, dental pain, labor pains, and trigeminal neuralgia. Homeopathic medicines must be customized to the individual patient in chronic conditions. Yet, a severe acute trauma can respond to the same homeopathic medicine in nearly all individuals. As an example, a standard protocol is provided to speed healing and reduce pain after surgery or dental extraction. While homeopathic medicines are rarely tested against conventional painkillers in a head-to-head trial, certain research studies show that homeopathic medicines can enhance healing for those already on conventional medications and can reduce pain in a condition such as a fracture for which effective drug treatment is lacking.

Abstract:

**Objective:** To evaluate the effectiveness and safety of Chinese herbal medicine Dengzhan Xixin (Erigeron breviscapus) injection for acute ischemic stroke.

**Design:** Systematic review and meta-analysis (CRD42016038413, http://www.crd.york.ac.uk/PROSPERO).

**Methods:** Six electronic databases were searched from inception to March 2016 for randomised controlled trials (RCTs) of Dengzhan Xixin (DZXX) injection for acute ischemic stroke. The methodological quality of RCTs was assessed by the Cochrane risk of bias tool.

**Data synthesis:** was performed using RevMan 5.3 and was presented with mean difference (MD) or relative risk (RR) and their 95% confidence interval (CI). A summary of finding table was generated by GRADEpro (version 3.6).

**Results:** Twenty-five RCTs with 2498 participants were included and all trials adopted conventional therapy (CT) in both arms. Most of the studies had high risk of bias. The addition of DZXX to CT showed no significant benefit on death (RR 0.27, 95% CI 0.05–1.63) within the treatment period (14–35 d), but showed higher Barthel index score (MD 10.20, 95% CI 8.16–12.25), lower neurological function deficit score (MD −3.99, 95% CI −5.68 to −2.30, by NFDS; MD −1.67, 95% CI −2.59 to −0.76, by NIHSS), and lower treatment failure (RR 0.40, 95% CI 0.31–0.52). Thirteen trials (52%) reported the outcome of adverse events, but no serious adverse events were reported.

**Conclusion:** Low quality evidence implied that DZXX injection appeared to improve neurological function in patients with acute ischemic stroke. However, this potential benefit should be further studied in large, rigorous trials.


Abstract:

**Introduction:** Virtual reality (VR) exercises have been investigated as a rehabilitation paradigm to reduce the risk of falling in the elderly. This study aimed to compare a VR program consisted of complex exercises and that of balance exercises.

**Methods:** The study was a single-blind, randomized, comparative trial conducted over 5 weeks. Twenty subjects over 65 years of age were divided into a complex exercise with virtual reality (CEVR) group and a balance exercise with virtual reality (BEVR) group. CEVR consisted of strengthening, flexibility, endurance, and balance exercises, while BEVR focused on balance exercises only. Before and after 10 times of 1 h training sessions, we measured isokinetic peak torque and total work of knee muscles using a dynamometer. The Timed Up & Go (TUG) test was also conducted to evaluate dynamic balance.
Results: Knee extension peak torque was significantly enhanced only in the CEVR group (p < 0.05), but there was no difference between groups. Both groups showed significant improvement of dynamic balance measured by TUG after training sessions, but the CEVR group exhibited greater improvement than the BEVR group (p < 0.05).

Conclusions: Our findings demonstrate the superiority of the virtual reality training with a complex exercise program to improve balance and muscle strength in the elderly when compared to the BEVR. As a training for prevention of falling in the elderly, we recommend a virtual reality program including various exercises for strength, endurance, balance, and flexibility.


Abstract:

Introduction: Auricular acupressure therapy is widely used in East Asia and Europe to prevent constipation in leukemia patients undergoing chemotherapy. The aim of this systematic review will be to evaluate the available evidence from randomized controlled trials (RCTs) of auricular acupressure therapy for preventing constipation in leukemia patients undergoing chemotherapy.

Methods: The following databases will be searched from their inception until May 2017: MEDLINE, CINAHL, EMBASE, AMED, the Cochrane Central Register of Controlled Trials and four Chinese databases [Chinese BioMedical Database (CBM), China National Knowledge Infrastructure (CNKI), Wan-Fang Data and Chinese WeiPu Database]. Only the RCTs related to the effects of auricular acupressure therapy on preventing constipation in leukemia patients undergoing chemotherapy will be included in this systematic review. A quantitative synthesis of RCTs will be conducted using RevMan 5.3 software. Study selection, data extraction, and validation will be performed independently by two reviewers. Cochrane criteria for risk-of-bias will be used to assess the methodological quality of the trials.

Ethics and dissemination: This systematic review will not use data from individual patients and no privacy issues will be violated. The results will be disseminated through peer-reviewed publications.

Trial registration number: PROSPERO registration number: CRD42017067880.


Abstract:

Objectives: Low back pain affects the person's ability to keep balance, especially in challenging conditions. The purpose of this study was to determine the immediate effects of Pilates exercises on postural sway and dynamic balance of young individuals with non-specific low back pain.

Design: Controlled laboratory design.
**Settings and main outcome measures:** Forty-six participants with non-specific low back pain were randomized to a Pilates (n = 23, 10 males; age: 21.8 ± 3.2 years) and a control group (n = 23, 9 males; age: 22.8 ± 3.6 years). Postural sway was assessed with a force platform and dynamic balance with the Star Excursion Balance Test, before and after the intervention or rest period. To assess postural sway, participants stood still on an unstable surface set on the force plate for 90s, with eyes closed.

**Intervention:** The intervention lasted 20 min and consisted on four Pilates exercises: single leg stretch (level 1), pelvic press (level 1), swimming (level 1) and kneeling opposite arm and leg reach.

**Results:** At baseline, no differences were found between groups. The Pilates group improved in all the postural sway values (area of CoP: 11.5 ± 3.4 to 9.7 ± 2.7 cm², p = 0.002 and CoP velocity: 2.8 ± 0.6 to 2.3 ± 0.5 cm/s, p < 0.001) and in the Star Excursion Balance Test. Control group only improved in CoP velocity, however, this improvement was significantly inferior compared to the Pilates group.

**Conclusions:** Pilates exercises immediately improved postural sway and dynamic balance in young adults with non-specific low back pain.


**Abstract:**

**Background:** Research has long suggested that a large and possibly growing number of people use complementary or alternative medicine (CAM). However, in many countries, such as Sweden, national and regional research on CAM use is still very limited. Existing prevalence studies are few and characterized by low comparability. This study aims to contribute towards addressing this knowledge gap.

**Methods:** A web-based survey measured the use of and attitude towards CAM and conventional medicine in the southernmost Swedish province of Scania, while taking part in the development of a measurement tool for the standardized study of CAM use within the European Union (EU; I-CAM-Q).

**Results:** 71% of the respondents (n = 1,534) reported having used some form of CAM in the past year. CAM consumption here includes visits to CAM providers, use of natural remedies, and use of self-help methods. Reported use was more common among women, younger age groups, and people with tertiary education. 69% of the respondents stated that collaboration between conventional medicine and complementary medicine should increase. The survey’s response rate was 31%.

**Conclusions:** The study confirms that CAM forms a considerable part of the health care offered to and used by the population. In the face of the existing lack of national and regional data on CAM usage, it affirms the importance of furthered investigation of CAM consumption, policy, practice, regulation, and education.


**Abstract:**
Objectives: Research demonstrates the benefits of complementary and alternative medicine (CAM) in myriad environments. Yet, the majority of CAM services are offered in outpatient settings. Incorporating CAM into hospital settings may lead to increased patient comfort, well-being, and overall satisfaction with hospital admissions. Few studies have examined CAM services among inpatients. Therefore, this study assessed inpatients’ preferences and beliefs regarding CAM, as well as their stated willingness to pay for these services.

Design: Adult patients (n = 100), ranging in age from 19–95 years (M = 53 years; SD = 19.2 years), were recruited during their hospitalization in the University of California, San Diego, Healthcare System. The inpatients completed a brief individual interview to gather their perspectives on common CAM services, including acupuncture, aromatherapy, art therapy, guided imagery, healthy food, humor therapy, massage therapy, music therapy, pet therapy, Reiki, and stress management. Inpatients were asked which CAM therapies they perceived as being potentially the most helpful, their willingness to pay for those therapies, and their perceived beliefs regarding the use of those therapies.

Results: Inpatients most commonly perceived healthy food (85%), massage therapy (82%), and humor therapy (70%) to be the most helpful, and were most willing to pay for healthy food (71%), massage therapy (70%), and stress management (48%). Inpatients most commonly believed CAM treatments would provide relaxation (88%), increase well-being (86%), and increase their overall satisfaction with the hospitalization (85%).

Conclusions: This study suggests that CAM services may be a beneficial addition to hospitals, as demonstrated by inpatients’ interest and stated willingness to pay for these services. These findings may help organizational leaders when making choices regarding the development of CAM services within hospitals, particularly since a significant percentage of inpatients reported that CAM services would increase their overall satisfaction with the hospitalization. These results merit further attention given the need to increase cost savings while enhancing the overall patient experience in today’s medical marketplace.


Abstract:

Background: Type 2 diabetes mellitus (T2DM) is a major global health problem. Though various studies have reported the beneficial effect of Yoga in patient with T2DM, there is a lack of study in combination with bell pepper and yoga. Hence, the present study aims at evaluating short-term effect of add on bell pepper juice with integrated approach of yoga therapy (IAYT) on blood glucose levels and cardiovascular variables in patients with T2DM.

Materials and methods: Fifty T2DM subjects with the age varied from 34 to 69-years were recruited and randomly divided into either study group or control group. The study group received 100-ml of bell pepper juice (twice/day) along with IAYT while the control group received only IAYT for 4-consecutive days. Baseline and post-test assessments
were taken before and after the intervention. Statistical analysis was performed using statistical package for the social sciences, version-16.

**Results:** Results of this study showed no significant difference in overall (fasting and post prandial) blood glucose level in the study group compared with control group. However, a significant reduction in Post prandial blood glucose (PPBG), systolic blood pressure (SBP), pulse pressure (PP), rate pressure product (RPP) and Double product (Do-P) was observed in the study group compared with control group.

**Conclusion:** Results of this study suggest that though an addition of 100-ml of bell pepper juice (twice/day) along with IAYT is not more effective in reducing fasting blood glucose, it may be more effective in reducing PPBG, SBP, PP, RPP and Do-P than IAYT alone.


**Abstract:**

Rosa damascena Mill. is one of the most famous ornamental plants cultivated all over the world mostly for perfumery industries. Traditionally it has been used as an astringent, analgesic, cardiac and intestinal tonic. The paucity of authoritative monographs urged us to summarize its clinical effectiveness and safety with a comprehensive review of the literature.

“PUBMED”, “SCOPUS”, “WEBOF SCIENCE” were searched up to April 30, 2017 with search terms: (“Rosa damascena” OR “Damask Rose”). All human studies with any mono-preparation were included. In vitro and animal studies from “PUBMED” were also reviewed and outlined.

Of “1000” identified publications, twelve eligible clinical trials were retrieved. Antimicrobial, anti-inflammatory, antioxidant, anticancer, protective neuronal, cardiac, gastrointestinal and hepatic effects in 30 in vitro and 21 animal studies were also shown. There are promising evidences for the effectiveness and safety of Rosa damascena Mill in pain relief, but confirmatory studies with standardized products is suggested.


**Abstract:**

**Aim:** To evaluate the effect of topical formulation of Rosa damascena Mill. (R. damascena) oil on migraine headache, applying syndrome differentiation model.

**Methods and materials:** Forty patients with migraine headache were randomly assigned to 2 groups of this double-blind, placebo-controlled cross-over trial. The patients were treated for the first 2 consecutive migraine headache attacks by topical R. damascena oil or placebo. Then, after one week of washout period, cross-over was done. Pain intensity of the patients' migraine headache was recorded at the beginning and ten-sequence time schedule of attacks up to 24 h. In addition, photophobia, phonophobia, and nausea and/or vomiting (N/V) of the patients were recorded as secondary
outcomes. Finally, gathered data were analysed in a syndrome differentiation manner to assess the effect of R. damascena oil on Hot- and Cold-type migraine headache.

**Results:** Mean pain intensity of the patients' migraine headache in the different time-points after R. damascena oil or placebo use, was not significantly different. Additionally, regarding mean scores of N/V, photophobia, and phonophobia severity of the patients, no significant differences between the two groups were observed. Finally, applying syndrome differentiation model, the mean score of migraine headache pain intensity turned out to be significantly lower in patients with “hot” type migraine syndrome at in 30, 45, 60, 90, and 120 min after R. damascena oil application compared to “cold” types (P values: 0.001, 0.001, <0.001, <0.001, and 0.02; respectively).

**Conclusion:** It seems that syndrome differentiation can help in selection of patients who may benefit from the topical R. damascena oil in short-term relief of pain intensity in migraine headache. Further studies of longer follow-up and larger study population, however, are necessitated for more scientifically rigorous judgment on efficacy of R. damascena oil for patients with migraine headache.


**Abstract:**

**Objective:** This study aimed to examine the effectiveness and safety of acupuncture in the treatment of Parkinson’s disease (PD).

**Methods:** English, Chinese, and Korean electronic databases were searched up to June 2016. Randomized controlled trials (RCTs) were eligible. The methodological quality was assessed using Cochrane’s risk of bias tool. Meta-analysis was performed using RevMan 5.3.

**Results:** In total, 42 studies involving 2625 participants were systematically reviewed. Participants treated using combined acupuncture and conventional medication (CM) showed significant improvements in total Unified PD Rating Scale (UPDRS), UPDRS I, UPDRS II, UPDRS III, and the Webster scale compared to those treated using CM alone. The combination of electroacupuncture and CM was significantly superior to CM alone in total UPDRS, UPDRS I, UPDRS II, and UPDRS IV. Similarly, the combination of scalp electroacupuncture, acupuncture, and CM was significantly more effective than CM alone in total UPDRS. However, our meta-analysis showed that the combination of electroacupuncture and CM was not significantly more effective than CM alone in UPDRS III, the Webster, and the Tension Assessment Scale. The results also failed to show that acupuncture was significantly more effective than placebo acupuncture in total UPDRS. Overall, the methodological quality of the RCTs was low. No serious adverse events were reported.

**Conclusions:** We found that acupuncture might be a safe and useful adjunctive treatment for patients with PD. However, because of methodological flaws in the included studies, conclusive evidence is still lacking. More rigorous and well-designed placebo-controlled trials should be conducted.

Abstract:

**Background:** Transcendental meditation (TM) is a stress reduction technique that can potentially lower blood pressure (BP) safely. The American Heart Association recommends that TM may be considered in clinical practice.

**Objective:** To provide an overview of all systematic reviews and meta-analyses of TM on BP for evidence-informed clinical decision making.

**Method:** Systematic searches of PubMed, EBSCOhost, Cochrane Library, Web of Science, Embase, and PsycINFO for all systematic reviews and/or meta-analyses of randomized controlled trials (RCTs) with TM as an intervention, and outcome measures include systolic BP (SBP) and diastolic BP (DBP). Qualitative and quantitative data were synthesized. The methodological quality of the selected reviews was assessed using the AMSTAR checklist.

**Results:** Eight systematic reviews and meta-analyses are included. Among them is an Agency for Healthcare Research and Quality report, a Cochrane systematic review, 4 independent reviews, and 2 reviews from a TM related institution. The quality of most of the included reviews is fair with a mean score of 5.75/11 on the AMSTAR scale. Overall, there exists a clear trend of increasing evidence over the years supporting the efficacy of TM in lowering BP. However, some conflicting findings remain across reviews and potential risk of bias exists in many of the RCTs included in these reviews.

**Conclusion:** Practising TM may potentially reduce the SBP by ~4 mm Hg and DBP by ~2 mm Hg. Such effect is comparable with other lifestyle interventions such as weight-loss diet and exercise. Further evidence from long-term well-designed RCTs conducted by independent researchers is needed.


Abstract:

The official acceptance of complementary and alternative medicine (CAM) or integrative medicine in the academic discussion and in health policies in Finland is still poor. This is in contradiction to the fact that modern Finnish citizens use CAM as much as any people elsewhere in the European Union, with rates of 28-46% of the general population, or even more. This was one of the reasons for the foundation of the Finnish Forum for Research in Integrative Medicine and Healthcare (SILF) in November 2014. A first challenge for the SILF was to facilitate a research seminar to address the issue of CAM research as a part of the Finnish academic research. The seminar was organized by the Department of Health Sciences of the University of Tampere on November 13, 2015.
Almost one third of the more than 400 participants were health professionals, and again one-third out of this group were physicians. As a result of the seminar, a research network was inaugurated. Obviously there is an increasing interest of health professionals in CAM and maybe even a change of attitude towards CAM also in Finland. However, genuine Finnish CAM research is essential in order to open up the academic discussion.


**Abstract:**

**Background:** The demand for complementary and alternative medicine (CAM) is rising. The German ‘Heilpraktiker’ is a non-medical naturopathic practitioner (NMNP) providing CAM. Their numbers are rising constantly; however, little is known about their practices and reasons for consultation and on what kind of treatment they offer.

**Methods:** All 1,096 NMNPs in the German federal state of Schleswig-Holstein were invited to participate in a questionnaire study to gain first insights into their nearly unexplored group setting.

**Results:** A total of 262 NMNPs responded to the itemized questionnaire; 60 answered the questionnaire suggested for non-responders. Out of the 262 NMNPs, 211 (81%) were female. The average age was 53 years. Analyzing the most frequent reasons for consultation, 68.2% were found to be general and unspecified reasons, followed by psychological causes (64.1%) and musculoskeletal complaints (53.1%). About 68% of the participants treat conditions of pain. The most commonly used group of methods was found to comprise para-medicinal procedures.

**Conclusions:** Our analysis gives first insights into the occupational profile of the German NMNPs, their scope of activities and treatment methods. It is a first step towards health service research that might provide a basis for further studies.


**Abstract:**

Aspergillosis is the name given to a wide variety of diseases caused by infection by fungi of the genus aspergillus. Allopathic treatment involves the use of antifungals for a prolonged period of time, due to the increasing resistance of these organisms to drug treatment. Homeopathic medicine offers an effective and safe therapeutic intervention for the complete resolution of this illness as described in the following case of a 54-year old male with drug resistant pulmonary aspergillosis.


Abstract:

Objectives: Posttraumatic stress disorder (PTSD) is a debilitating condition that affects many who have experienced trauma. In addition to skills-focused treatments, exposure-based treatments, cognitive therapy, combination treatments, and EMDR, a number of alternative treatments for PTSD have emerged in recent years. The search for alternative treatments is justified based on the empirical observation that a large percentage of individuals fail to benefit optimally from existing treatments (e.g., between 30 and 60). Moreover, current studies often utilize stringent inclusion criteria (e.g., absence of comorbid disorders), raising the likelihood that results will not generalize to many individuals currently experiencing PTSD. The primary objective of the current paper was to explore the effects of one type of alternative treatment: yoga.

Design: A comprehensive review of the literature was conducted targeting research examining yoga postures and PTSD. Seven randomized controlled trials (RCTs) were identified and reviewed, and effect sizes were computed for the post-test assessments.

Results: Cohen's d for each study ranged (in absolute value) from a low of −0.06 to a high of 1.42 (average weighted d across studies was 0.48; 95% CI: 0.26, 0.69).

Conclusions: Putative mechanisms of action for the possible beneficial effects of yoga for PTSD-related symptomatology and clinical implications are discussed.


Abstract:

Objectives: Vasomotor symptoms (VMS), commonly reported during menopausal transition, negatively affect psychological health and health-related quality of life (HRQoL). While hormone therapy is an effective treatment, its use is limited by concerns about possible harms. Thus, many women with VMS seek nonhormonal, nonpharmacologic treatment options. However, evidence to guide clinical recommendations is inconclusive. This study reviewed the effectiveness of yoga, tai chi and qigong on vasomotor, psychological symptoms, and HRQoL in peri- or post-menopausal women.

Design: MEDLINE, Cochrane Database of Systematic Reviews, EMBASE, CINAHL and the Allied and Complementary Medicine Database were searched. Researchers identified systematic reviews (SR) or RCTs that evaluated yoga, tai chi, or qigong for vasomotor, psychological symptoms, and health-related quality of life (HRQoL) in peri- or post-menopausal women. Data were abstracted on study design, participants, interventions and outcomes. Risk of bias (ROB) was assessed and updated meta-analyses were performed.
Results: We identified one high-quality SR (5 RCTs, 582 participants) and 3 new RCTs (345 participants) published after the SR evaluating yoga for vasomotor, psychological symptoms, and HRQoL; no studies evaluated tai chi or qigong. Updated meta-analyses indicate that, compared to controls, yoga reduced VMS (5 trials, standardized mean difference (SMD) −0.27, 95% CI −0.49 to −0.05) and psychological symptoms (6 trials, SMD −0.32; 95% CI −0.47 to −0.17). Effects on quality of life were reported infrequently. Key limitations are that adverse effects were rarely reported and outcome measures lacked standardization.

Conclusions: Results from this meta-analysis suggest that yoga may be a useful therapy to manage bothersome vasomotor and psychological symptoms.


Abstract:

Introduction: Dementia is a common, progressive disorder impairing brain function and affecting both sufferers and caregivers’ wellbeing. The number of dementia patients will increase as the population ages. Rosmarinic acid is a natural compound with choline esterase inhibitory potency found in members of the botanical family lamiaceae, including sage, rosemary, and lemon balm, and has been suggested as having potential efficacy as a dementia intervention. This study aimed to evaluate effectiveness of these herbs based on a review of randomised controlled trials.

Methods: Database searches were conducted separately for each herb using PubMed, the Cochrane Library, and ScienceDirect for clinical evidence for sage (Salvia officinalis L. or S. lavandulaefolia Vahl), rosemary (Rosmarinus officinalis L.), and lemon balm (Melissa officinalis L.), administered individually.

Results: Database searching identified 235, 112, and 177 articles for sage, rosemary, and lemon balm, respectively. From these, eight studies for sage, five for rosemary and eight for lemon balm met the inclusion criteria. Trials were analysed based on the study designs and summarized as narrative synthesis as data were heterogeneous in terms of the target populations, herbal preparations and administration methods.

Studies suggested sage spp. could improve cognitive performance and alertness. Rosemary could improve cognitive performance and alertness. Among eight articles identified on lemon balm, seven studies found it effective in improving mood or cognition. One study found no effect.

Conclusions: Some clinical evidence supports the benefit of these herbs in dementia intervention. However, methodological heterogeneity and variable trial quality made information synthesis difficult. Further research is required to determine dosage and intervention periods.


Abstract:
**Introduction:** This article shares the findings of a preliminary survey undertaken for the Ministry of Health in Turkey to help develop their policies on the use of Traditional and Complementary Medicine (T&CM). The primary aim was to find out how T&CM is used by the patients as a part of their treatment processes and also to find out whether some practices that are not included in the Western description of T&CM are in common use in Turkey and their cultural implications.

**Methods:** This cross-sectional, paper-based questionnaire survey was carried out in 39 public hospitals and 21 general practice clinics within seven geographical areas of Turkey. Patients in the waiting rooms with an appointment on that particular day were included.

**Results:** 2770 women (47.1%) and 3112 men (52.9%) participated in the survey. The overall T&CM use was 60.5%. Women's frequency of T&CM use was higher than men ($P = 0.001$). Strong gender component of T&CM use needs further quantitative research taking cultural aspects into consideration. 59.4% of the participants who used T&CM reported that it was recommended to them by others and only 54.3% shared information about their use of T&CM with their physicians. Leech therapy and cupping prevalence was higher in Turkey compared to other countries possibly due to religious and cultural beliefs.

**Conclusion:** The frequency of T&CM use is high which was a reflection of belief-based therapeutic approaches in other words, there is a divide between traditional medicine and complementary and alternative medicine in Turkey, which needs to be separately evaluated.


**Abstract:**

**Objectives:** To understand depressed individuals’ experiences in a 10-week hatha yoga program.

**Design:** In a randomized controlled trial, participants were assigned to either 10 weeks of hatha yoga classes or a health education control group. This report includes responses from participants in yoga classes. At the start of classes, average depression symptom severity level was moderate.

**Main outcome measures:** After 10 weeks of yoga classes, we asked participants ($n = 50$) to provide written responses to open-ended questions about what they liked about classes, what they did not like or did not find helpful, and what they learned. We analyzed qualitative data using thematic analysis.
**Results and conclusions:** Elements of yoga classes that may increase acceptability for depressed individuals include having instructors who promote a non-competitive and non-judgmental atmosphere, who are knowledgeable and able to provide individualized attention, and who are kind and warm. Including depression-related themes in classes, teaching mindfulness, teaching breathing exercises, and providing guidance for translating class into home practice may help to make yoga effective for targeting depression. Participants’ comments reinforced the importance of aspects of mindfulness, such as attention to the present moment and acceptance of one’s self and one’s experience, as potential mechanisms of action. Other potential mechanisms include use of breathing practices in everyday life and the biological mechanisms that underlie the positive impact of yogic breathing. The most serious concern highlighted by a few participants was the concern that the yoga classes were too difficult given their physical abilities.


**Abstract:**

**Objective:** To explore the effect of acupuncture on common extensor tendon (CET) thickness in patients with lateral epicondylitis (LE). Additionally, to identify whether clinical and ultrasonographic changes showed any correlation.

**Methods:** Forty-one patients were randomly assigned to acupuncture and control groups. Conventional treatment (rest, NSAİİ, bracing, exercise) methods for LE were applied to all patients. In addition to this, the acupuncture treatment was applied to the acupuncture group. The visual analog scale (VAS) for pain, the Duruoz Hand Index (DHI) for functioning of the affected limb, the pressure pain threshold, and CET thickness (via ultrasound imaging) were assessed before and end of the treatment in both groups.

**Results:** The VAS and DHI scores in both groups decreased. The pressure pain threshold and CET thickness only demonstrated improvement in the acupuncture group.

**Conclusion:** These findings show that the CET thickness was reduced after 10 sessions of acupuncture treatment in LE patients.


**Abstract:**

**Introduction:** Depression is one of the clinical conditions patients most commonly consult homeopaths. This study therefore aimed to learn about patients’ experiences having this intervention.

**Methods:** A semi-structured qualitative interview study was nested within a randomised controlled trial to learn about depressed patients’ experiences with treatment provided by homeopaths. A purposive selection of adults with moderate to severe self-reported
depression were included. Interviews were conducted post initial consultation and six months post-randomisation. Thematic analysis was used to develop themes describing participants’ experiences, thoughts and understandings.

**Results:** Forty-six interviews were carried out with 33 adults. Sixteen themes were developed and have been categorised under three main headings: 1) changed understanding of the intervention, with themes such as understanding the intervention as being adapted; 2) experiences with the consultation and the medication, such as caring support, trust and optimism arising from consultations with homeopaths; and 3) changes in state of health, such as improvement in mood, wellbeing and ability to cope, or little or no change, or transient adverse events.

**Conclusion:** This is the first qualitative study of depressed patients’ experiences with treatment provided by homeopaths. Results provide an insight into their experiences with consultations and homeopathic and antidepressant medication, their understanding of the intervention, and the changes in their state of health over time.


**Abstract:**

**Objective:** Indigenous people’s ceremonies using rhythm and dance have been used for countless generations throughout the world for healing, conflict resolution, social bonding, and spiritual experience. A previous study reported that a ceremony based on the Central African ngoma tradition was favorably received by a group of Americans. The present trial compared the effects of the modified ngoma ceremony (Ngoma) with those of mindfulness-based stress reduction (MBSR) in a randomized pilot study.

**Methods:** Twenty-one women were randomized to either Ngoma or MBSR. Both groups had sessions on a weekly basis for 8 weeks and completed questionnaires at baseline, week 8, and 1 month after the intervention. Participants completed questionnaires, which included self-report of depressive and anxiety symptoms, health status (e.g., quality of life and functioning), social bonding, and perception of the credibility of the two interventions.

**Results:** Both groups showed improvements in depression, anxiety, emotional well being, and social functioning as measured by respective scales. Social bonding also increased in both groups during the study and may be a mechanism for both interventions. Participants found both interventions credible.

**Conclusions:** In this pilot study, Ngoma showed significant and durable beneficial effects comparable to MBSR. The effects of Ngoma and other indigenous rhythm-dance ceremonies on distress and health status in western culture should be investigated in larger clinical studies.


**Abstract:**
**Objectives:** GuiZhi-ShaoYao-ZhiMu decoction (GSZD), a traditional Chinese herbal medication for the management of rheumatoid arthritis (RA), has a long history of use and modern scientific research support for efficacy, but the studies have not been systematically evaluated. Therefore, this study systematically reviewed the efficacy of GSZD using the available human clinical trials and conducted a meta-analysis.

**Methods:** The available databases were searched using proper languages of English, Korean, and Chinese. The key terms used for searching were “GSZD,” “Cassia Twig,” “Guizhi,” “Paeonia lactiflora,” “Shaoyao,” “Anemarrhena Rhizome,” “Zhimu,” “rheumatoid arthritis,” “randomized,” “controlled trial,” and “clinical trial.” Randomized clinical trials (RCTs) using GSZD were included in the review and meta-analysis. According to heterogeneity, odds ratio and confidence intervals in the pooled RCTs were assessed by a fixed or random model in meta-analysis. Risk of bias was evaluated for all included studies.

**Results:** Thirteen RCTs met the inclusion criteria and were included in the meta-analysis. All studies evaluated the efficacy of GSZD for treating RA, but the herbal formulations varied since some studies added herbs to the basic GSZD formulation. However, all formulations contained the essential herbs: Guizhi, Shaoyao, and Zhimu. Each RCT included an experimental group (GSZD with or without Western-style medicine) and a control group (either standard Western-style medicines or placebo). When compared to placebo, the GSZD treatment was found to be three to six times more effective than standard Western drugs for some symptoms. Furthermore, only two studies reported any adverse events associated with the GSZD group, whereas several reported serious adverse events in the control groups.

**Conclusions:** The Traditional Chinese Medicine, GSZD, may have equal or superior effectiveness and safety for treating RA compared to Western RA drugs. It should be considered a viable alternative to Western medicine. However, more long-term research is needed in larger patient groups to better establish its safety and efficacy.


**Abstract:**

The Delhi Government Homeopathic Dispensary, a primary health care center in Aali Village, New Delhi, witnessed a sporadic surge in cases of mumps during the months of May and June 2015. The cases were treated successfully using different homeopathic medicines prescribed according to the Law of Similar.


**Abstract:**

**Introduction:** Insomnia can occur independently or in conjunction with other diseases, with the common symptom of poor sleep quantity and/or decreasing time asleep. In Chinese medicine, the acu-point HT7 along heart meridian is a very important acu-point for treating insomnia, however no systematic reviews have been carried out to evaluate the effectiveness of stimulating HT7 as a single point for treating insomnia.
Methods: A literature search of English and Chinese databases was carried out for randomized controlled trials evaluating the stimulation of HT7 as a sole acu-point for insomnia (irrespective of cause) compared with routine care or placebo. Trial reporting quality was assessed using the Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) checklist and the Cochrane Risk of Bias Tool (PROSPERO registration number: CRD42016036191).

Results: Four trials involving 436 participants were included. All trials were limited in their reporting and methodological quality. Statistically significant improvements were shown for HT7 simulation used for patients with insomnia who had coronary heart disease (measured by improvement ratio), and the simulation included acupressure (P < 0.05) and moxa (x² = 18.98, P < 0.01); Statistically improvements were shown for HT7 acupressure used for insomnia occurred independently (measured by anxiety questionnaires – a sensation of wellbeing and urinary sulphate-melatonin evaluation). No trial reported any adverse events.

Conclusions: There was insufficient evidence to confirm whether HT7 stimulation could improve insomnia but there are some positive indications which warrant further research. These findings should be interpreted with caution due to the poor reporting and methodological quality of included trials.


Abstract:

Objective: To study nausea, vomiting and need for rescue antiemetics in patients receiving antiemetic acupuncture, sham acupuncture or standard care during concomitant chemotherapy during pelvic radiotherapy.

Methods: In total, 68 patients participated (75% women, mean age 56 years, 53% had gynecological, 43% colorectal, and 4% other cancer types). Fifty-seven of them were blinded randomized to verum (n = 28) or sham (n = 29) acupuncture, median 10 sessions. During the study period of four weeks, the patients daily registered their nausea, vomiting and consumption of antiemetics. They were compared to a reference group (n = 11) receiving standard care only, who delivered these data once (after receiving mean 27 Gy radiotherapy dose).

Results: More patients in the sham acupuncture group (17 of 20; 85%, p = 0.019, RR 1.81, CI 1.06–3.09) consumed antiemetics, compared to the verum acupuncture group (8 of 17; 47%). In the standard care group, 7 of 11 (63%) consumed antiemetics. The verum acupuncture treated patients experienced lower intensity of nausea than the other patients (p = 0.049). There was a non-significant tendency that more patients receiving either sham acupuncture or standard care experienced nausea (21 of 31; 68%) than patients receiving verum acupuncture (9 of 17; 53%: p = 0.074, RR 1.58, CI 0.91–2.74).

Conclusion: Patients treated with verum acupuncture needed less antiemetics and experienced milder nausea than other patients. Our study was small and many analyses
lacked statistical power to detect differences; we welcome further sham-controlled efficacy studies and studies regarding the role of non-specific treatment components for experiencing antiemetic effects of acupuncture.


**Abstract:**

Many herbs and herbal formulas are effective for migraine sufferers, both as acute treatment and for prevention, particularly when coupled with the identification and elimination of migraine triggers. The natural products discussed here include *Zingiber officinale* (ginger) for migraine treatment and *Cannabis sativa* (cannabis), intranasal *Capsicum annum* (cayenne), and *Lavandula stoechas* (Spanish lavender) volatile oil for treatment and prevention. The many agents discussed for migraine prevention primarily include *Petasites hybridus* (butterbur) root, *Curcuma longa* (turmeric)+fish oil, *Citrus medica* (citron) fruit, *Tanacetum parthenium* (feverfew), *Tanacetum parthenium* (feverfew)+*Salix alba* (white willow), *Ginkgo biloba* (ginkgo), and *Lippia alba* (bushy matgrass), though the latter three have little published evidence of efficacy. The Chinese herbal formulas *Zhèng Tiān Wán* (Rectify Heaven Pill) and *Wú Zhū Yú Tāng* (Evodia Decoction, goshuyutō) have fairly strong evidence supporting their efficacy for migraine prophylaxis. Dosing and safety information are provided for all herbs discussed.
Allied System


Abstract:
**Background:** Exenatide, a glucagon-like peptide-1 (GLP-1) receptor agonist, has neuroprotective effects in preclinical models of Parkinson’s disease. We investigated whether these effects would be apparent in a clinical trial.

**Methods:** In this single-centre, randomised, double-blind, placebo-controlled trial, patients with moderate Parkinson’s disease were randomly assigned (1:1) to receive subcutaneous injections of exenatide 2 mg or placebo once weekly for 48 weeks in addition to their regular medication, followed by a 12-week washout period. Eligible patients were aged 25–75 years, had idiopathic Parkinson’s disease as measured by Queen Square Brain Bank criteria, were on dopaminergic treatment with wearing-off effects, and were at Hoehn and Yahr stage 2·5 or less when on treatment. Randomisation was by web-based randomisation with a two strata block design according to disease severity. Patients and investigators were masked to treatment allocation. The primary outcome was the adjusted difference in the Movement Disorders Society Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) motor subscale (part 3) in the practically defined off-medication state at 60 weeks. All efficacy analyses were based on a modified intention-to-treat principle, which included all patients who completed any post-randomisation follow-up assessments. The study is registered at ClinicalTrials.gov (NCT01971242) and is completed.

**Findings:** Between June 18, 2014, and March 13, 2015, 62 patients were enrolled and randomly assigned, 32 to exenatide and 30 to placebo. Our primary analysis included 31 patients in the exenatide group and 29 patients in the placebo group. At 60 weeks, off-medication scores on part 3 of the MDS-UPDRS had improved by 1·0 points (95% CI −2·6 to 0·7) in the exenatide group and worsened by 2·1 points (−0·6 to 4·8) in the placebo group, an adjusted mean difference of −3·5 points (−6·7 to −0·3; p=0·0318). Injection site reactions and gastrointestinal symptoms were common adverse events in both groups. Six serious adverse events occurred in the exenatide group and two in the placebo group, although none in either group were judged to be related to the study interventions.

**Interpretation:** Exenatide had positive effects on practically defined off-medication motor scores in Parkinson’s disease, which were sustained beyond the period of exposure. Whether exenatide affects the underlying disease pathophysiology or simply induces long-lasting symptomatic effects is uncertain. Exenatide represents a major new avenue for investigation in Parkinson’s disease, and effects on everyday symptoms should be examined in longer-term trials.

**Funding:** Michael J Fox Foundation for Parkinson’s Research.


**Abstract:**

**Introduction:** Nutritional therapy (NT) since the mid-1980s has undergone a process of professional, regulatory and educational development. To inform the continuance of this process the Nutritional Therapy Education Commission (NTEC) initiated an exploration of practitioner profiles. The aim was to ensure NTEC are meeting these developmental requirements by: informing a revised Core Curriculum; ensuring an evidence-based approach to professional training; establishing appropriateness of ‘fit’ between
qualification and subsequent occupation and clarifying possible barriers to, or reasons for non-continuance of practice.

**Methods:** An anonymous online survey recruited 408 qualified nutritional therapists in the UK. Numerical data were analysed descriptively and statistically using SPSS (Statistical Package for the Social Science).

**Results:** The majority of the respondents were female, aged between 31 and 50 years and working part time, in self-employed clinical practice; almost a third of these earning a primary income. The current training provision appears to be adequate, however further training needs were identified. Barriers to practice maybe income driven or personal for a minority, however further research is needed. The majority were registered with the voluntary regulator and were members of a professional body with a range of continuing professional development strategies. Functional medicine approaches were reported to be widely incorporated into practice and awareness of the role of nutrigenomics was common, but clinical application of nutrigenetic testing was less widespread.

**Conclusion:** The findings suggest that in the captured population current NT education and professional provision results in clinical practice however there are areas for further development.

**Bent Martin J van den, Baumert Brigitta, Erridge Sara C et al. Interim results from the CATNON trial (EORTC study 26053-22054) of treatment with concurrent and adjuvant temozolomide for 1p/19q non-co-deleted anaplastic glioma: A phase 3, randomised, open-label intergroup study. Lancet 2017; 390(10103): 1645-53p.**

**Abstract:**

**Background:** The role of temozolomide chemotherapy in newly diagnosed 1p/19q non-co-deleted anaplastic gliomas, which are associated with lower sensitivity to chemotherapy and worse prognosis than 1p/19q co-deleted tumours, is unclear. We assessed the use of radiotherapy with concurrent and adjuvant temozolomide in adults with non-co-deleted anaplastic gliomas.

**Methods:** This was a phase 3, randomised, open-label study with a $2 \times 2$ factorial design. Eligible patients were aged 18 years or older and had newly diagnosed non-co-deleted anaplastic glioma with WHO performance status scores of 0–2. The randomisation schedule was generated with the electronic EORTC web-based ORTA system. Patients were assigned in equal numbers (1:1:1:1), using the minimisation technique, to receive radiotherapy (59·4 Gy in 33 fractions of 1·8 Gy) alone or with adjuvant temozolomide (12 4-week cycles of 150–200 mg/m2 temozolomide given on days 1–5); or to receive radiotherapy with concurrent temozolomide 75 mg/m2 per day, with or without adjuvant temozolomide. The primary endpoint was overall survival adjusted for performance status score, age, 1p loss of heterozygosity, presence of oligodendrogial elements, and MGMT promoter methylation status, analysed by intention to treat. We did a planned interim analysis after 219 (41%) deaths had occurred to test the null hypothesis of no efficacy (threshold for rejection $p<0·0084$). This trial is registered with ClinicalTrials.gov, number NCT00626990.

**Findings:** At the time of the interim analysis, 745 (99%) of the planned 748 patients had been enrolled. The hazard ratio for overall survival with use of adjuvant temozolomide was 0·65 (99·145% CI 0·45–0·93). Overall survival at 5 years was 55·9% (95% CI 47·2–63·8) with and 44·1% (36·3–51·6) without adjuvant temozolomide. Grade 3–4 adverse events were seen in 8–12% of 549 patients assigned temozolomide, and were mainly haematological and reversible.
**Interpretation:** Adjuvant temozolomide chemotherapy was associated with a significant survival benefit in patients with newly diagnosed non-co-deleted anaplastic glioma. Further analysis of the role of concurrent temozolomide treatment and molecular factors is needed.

**Funding:** Schering Plough and MSD.


**Abstract:**

**Objective:** Arthrocentesis and prolotherapy are nonsurgical treatments for temporomandibular joint (TMJ) diseases. This study aimed to evaluate the treatment of hypermobility, pain, and displacement of the TMJ by consecutively performing arthrocentesis and prolotherapy in the same session.

**Materials and Methods:** In this study, 10 adults with disc displacement and painful, hypermobile TMJ were selected. Arthrocentesis and prolotherapy were consecutively performed using a 30% dextrose solution that was simultaneously injected into five areas: posterior disc attachment, superior joint space, superior and inferior capsular attachments, and stylomandibular ligament. Paired t-test, McNemar test, and chi-square test were used to assess the maximum mouth opening, clicking sounds, pain, and subluxation of the TMJ. Patients with rheumatoid arthritis and parafunctional habits such as teeth clenching and grinding and biting of the cheeks or any other objects and those who had undergone surgery were excluded from this study.

**Results:** A total of 10 participants (36.20 ± 7.06 years old, 7 women and 3 men) received a single treatment session of combined arthrocentesis and prolotherapy at the same office visit. Subluxation frequency and pain significantly decreased after the first week of treatment (p < 0.05). Subluxation also decreased at the 3-month follow-up (p < 0.05). Clicking sound values did not significantly change at any of the follow-up time points. Maximum mouth opening values decreased at all follow-up time points compared to baseline (p < 0.05).

**Conclusion:** A single session of combined arthrocentesis and prolotherapy to treat symptomatic TMJ safely and significantly improved the subluxation and pain after 1 week and subluxation after 3 months compared to baseline status. The maximum mouth opening significantly decreased at all follow-up time points. Future studies assessing multiple treatment sessions are warranted.

Abstract:

**Background:** Rucaparib, a poly(ADP-ribose) polymerase inhibitor, has anticancer activity in recurrent ovarian carcinoma harbouring a BRCA mutation or high percentage of genome-wide loss of heterozygosity. In this trial we assessed rucaparib versus placebo after response to second-line or later platinum-based chemotherapy in patients with high-grade, recurrent, platinum-sensitive ovarian carcinoma.

**Methods:** In this randomised, double-blind, placebo-controlled, phase 3 trial, we recruited patients from 87 hospitals and cancer centres across 11 countries. Eligible patients were aged 18 years or older, had a platinum-sensitive, high-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube carcinoma, had received at least two previous platinum-based chemotherapy regimens, had achieved complete or partial response to their last platinum-based regimen, had a cancer antigen 125 concentration of less than the upper limit of normal, had a performance status of 0–1, and had adequate organ function. Patients were ineligible if they had symptomatic or untreated central nervous system metastases, had received anticancer therapy 14 days or fewer before starting the study, or had received previous treatment with a poly(ADP-ribose) polymerase inhibitor. We randomly allocated patients 2:1 to receive oral rucaparib 600 mg twice daily or placebo in 28 day cycles using a computer-generated sequence (block size of six, stratified by homologous recombination repair gene mutation status, progression-free interval after the penultimate platinum-based regimen, and best response to the most recent platinum-based regimen). Patients, investigators, site staff, assessors, and the funder were masked to assignments. The primary outcome was investigator-assessed progression-free survival evaluated with use of an ordered step-down procedure for three nested cohorts: patients with BRCA mutations (carcinoma associated with deleterious germline or somatic BRCA mutations), patients with homologous recombination deficiencies (BRCA mutant or BRCA wild-type and high loss of heterozygosity), and the intention-to-treat population, assessed at screening and every 12 weeks thereafter. This trial is registered with ClinicalTrials.gov, number NCT01968213; enrolment is complete.

**Findings:** Between April 7, 2014, and July 19, 2016, we randomly allocated 564 patients: 375 (66%) to rucaparib and 189 (34%) to placebo. Median progression-free survival in patients with a BRCA-mutant carcinoma was 16·6 months (95% CI 13·4–22·9; 130 [35%] patients) in the rucaparib group versus 5·4 months (3·4–6·7; 66 [35%] patients) in the placebo group (hazard ratio 0·23 [95% CI 0·16–0·34]; p < 0·0001). Across all primary analysis groups, rucaparib significantly improved progression-free survival in patients with platinum-sensitive ovarian cancer who had achieved a response to platinum-based chemotherapy. ARIEL3 provides further evidence that use of a poly(ADP-ribose) polymerase inhibitor in the maintenance treatment setting versus placebo could be considered a new standard of care for women with platinum-sensitive ovarian cancer following a complete or partial response to second-line or later platinum-based chemotherapy.

**Interpretation:** Across all primary analysis groups, rucaparib significantly improved progression-free survival in patients with platinum-sensitive ovarian cancer who had achieved a response to platinum-based chemotherapy. ARIEL3 provides further evidence that use of a poly(ADP-ribose) polymerase inhibitor in the maintenance treatment setting versus placebo could be considered a new standard of care for women with platinum-sensitive ovarian cancer following a complete or partial response to second-line or later platinum-based chemotherapy.


Abstract:
Systemic sclerosis, also called scleroderma, is an immune-mediated rheumatic disease that is characterised by fibrosis of the skin and internal organs and vasculopathy. Although systemic sclerosis is uncommon, it has a high morbidity and mortality. Improved understanding of systemic sclerosis has allowed better management of the disease, including improved classification and more systematic assessment and follow-up. Additionally, treatments for specific complications have emerged and a growing evidence base supports the use of immune suppression for the treatment of skin and lung fibrosis. Some manifestations of the disease, such as scleroderma renal crisis, pulmonary arterial hypertension, digital ulceration, and gastro-oesophageal reflux, are now treatable. However, the burden of non-lethal complications associated with systemic sclerosis is substantial and is likely to become more of a challenge. Here, we review the clinical features of systemic sclerosis and describe the best practice approaches for its management. Furthermore, we identify future areas for development.


Abstract:

**Objective:** The study objectives were to characterize botanical dietary supplement (BDS) use and to compare the motivations for botanical supplement (BS) use to the efficacy of the botanical in a socioeconomically and racially diverse urban adult population.

**Methods:** Subjects were from the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study, a 20-year prospective health disparities study with African American and white adults from Baltimore, Maryland. All study participants completed two dietary recalls and a dietary supplement (DS) questionnaire in Wave 3 (n = 2140). Diet quality was evaluated by the Healthy Eating Index-2010 and the Mean Adequacy Ratio for 17 micronutrients. A comparison of reported motivations to efficacy reported in the literature of single BS was conducted.

**Results:** Approximately 50% (1062/2140) of participants took DS. Of these, 8% (n = 178) reported taking either BS or BDS. It was found that BDS users had better diet quality than DS users as well as nonusers of DS. The top three motivations for BDS users were to improve overall health, to maintain health, and to supplement the diet. There is limited evidence for the efficacy of most BS. Review of the efficacy of the 15 BS reported by ≥5% of the study population revealed beneficial health roles for only fiber, gingko biloba extract EGB 761, and hawthorn berry.

**Conclusion:** To the authors’ knowledge, this study is the first to report a better quality diet with BDS use for a racially diverse urban population. Yet, improvement in diet is needed because overall quality did not achieve current recommendations. To improve overall health, it may be beneficial for this population to focus on dietary modifications to reduce the risks associated with chronic diseases. In general, the reported motivations for BS use were not supported by clinical evidence.


Enblom Anna, Steineck Gunnar, Borjeson Sussanne. Complementary and alternative medicine self-care strategies for nausea in patients undergoing abdominal or pelvic irradiation for cancer: A longitudinal observational study of

Abstract:

Objective: To longitudinally describe practice of Complementary and Alternative Medicine (CAM) self-care strategies for nausea during radiotherapy.

Methods: Two hundred patients daily registered nausea and practice of CAM self-care strategies, beside conventional antiemetic medications, for nausea during abdominal/pelvic irradiation (median five weeks) for gynecological (69%) colorectal (27%) or other tumors (4%).

Results: During radiotherapy, 131 (66%) experienced nausea, and 50 (25%) practiced self-care for nausea at least once, for a mean (m) of 15.9 days. The six of 50 patients who stayed free from nausea practiced self-care more frequent (m = 25.8 days) than the 44 patients experiencing nausea (m = 14.5) (p = 0.013). The CAM self-care strategies were: modifying eating (80% of all self-care practicing patients, 80% of the nauseous patients versus 83% of the patients free from nausea; ns) or drinking habits (38%, 41% vs 17%; ns), taking rests (18%, 20% vs 0%; ns), physical exercising (6%, 2% vs 33%; p = 0.035), acupressure (4%, 5% vs 0%; ns) and self-induced vomiting (2%, 2% vs 0%; ns).

Conclusion: A fourth of patients undergoing emetogenic radiotherapy practiced CAM self-care for nausea, mostly by modifying eating or drinking habits. The CAM self-care practicing patients who did not become nauseous practiced self-care more frequent than the nauseous patients did. To make such self-care evidence based, we need studies evaluating its efficacy.


Abstract:

Background: Documentation of the demographic and geographical details of changes in cause-specific neonatal (younger than 1 month) and 1–59-month mortality in India can guide further progress in reduction of child mortality. In this study we report the changes in cause-specific child mortality between 2000 and 2015 in India.

Methods: Since 2001, the Registrar General of India has implemented the Million Death Study (MDS) in 1·3 million homes in more than 7000 randomly selected areas of India. About 900 non-medical surveyors do structured verbal autopsies for deaths recorded in these homes. Each field report is assigned randomly to two of 404 trained physicians to classify the cause of death, with a standard process for resolution of disagreements. We combined the proportions of child deaths according to the MDS for 2001–13 with annual UN estimates of national births and deaths (partitioned across India’s states and rural or urban areas) for 2000–15. We calculated the annual percentage change in sex-specific and cause-specific mortality between 2000 and 2015 for neonates and 1–59-month-old children.

Findings: The MDS captured 52252 deaths in neonates and 42057 deaths at 1–59 months. Examining specific causes, the neonatal mortality rate from infection fell by 66% from 11·9 per 1000 livebirths in 2000 to 4·0 per 1000 livebirths in 2015 and the rate from birth asphyxia or trauma fell by 76% from 9·0 per 1000 livebirths in 2000 to 2·2 per 1000 livebirths in 2015. At 1–59 months, the mortality rate from pneumonia fell by 63% from
11.2 per 1000 livebirths in 2000 to 4.2 per 1000 livebirths in 2015 and the rate from diarrhoea fell by 66% from 9.4 per 1000 livebirths in 2000 to 3.2 per 1000 livebirths in 2015 (with narrowing girl–boy gaps). The neonatal tetanus mortality rate fell from 1.6 per 1000 livebirths in 2000 to less than 0.1 per 1000 livebirths in 2015 and the 1–59-month measles mortality rate fell from 3.3 per 1000 livebirths in 2000 to 0.3 per 1000 livebirths in 2015. By contrast, mortality rates for prematurity or low birthweight rose from 12.3 per 1000 livebirths in 2000 to 14.3 per 1000 livebirths in 2015, driven mostly by increases in term births with low birthweight in poorer states and rural areas. 29 million cumulative child deaths occurred from 2000 to 2015. The average annual decline in mortality rates from 2000 to 2015 was 3.3% for neonates and 5.4% for children aged 1–59 months. Annual declines from 2005 to 2015 (3.4% decline for neonatal mortality and 5.9% decline in 1–59-month mortality) were faster than were annual declines from 2000 to 2005 (3.2% decline for neonatal mortality and 4.5% decline in 1–59-month mortality). These faster declines indicate that India avoided about 1 million child deaths compared with continuation of the 2000–05 declines.

**Interpretation:** To meet the 2030 Sustainable Development Goals for child mortality, India will need to maintain the current trajectory of 1–59-month mortality and accelerate declines in neonatal mortality (to >5% annually) from 2015 onwards. Continued progress in reduction of child mortality due to pneumonia, diarrhoea, malaria, and measles at 1–59 months is feasible. Additional attention to low birthweight is required.


**Abstract:**

**Objectives:** Postpartum hemorrhage (PPH) is one of three main causes of maternal mortality and a life-threatening condition throughout the world. PPH can have irreversible complications for the mother even if it does not lead to death. This study was conducted to determine the effect of hydroalcoholic extract of Capsella bursa pastoris on early PPH.

**Design:** The present study was a single-blinded, randomized, clinical trial.

**Setting:** The study was conducted in Afzalipour Hospital of Kerman in 2015.

**Subjects:** The subjects included 100 women who had given vaginal birth and met the study inclusion criteria.

**Intervention:** The participants were selected and randomly assigned into an intervention group (n = 50) and a placebo group (n = 50). Immediately after placental expulsion, the intervention group was given 10 sublingual drops of the hydroalcoholic extract of Capsella bursa pastoris plus an infusion of 20 U of oxytocin in 1 L of Ringer’s solution, and the control group was given 10 sublingual drops of the placebo plus an infusion of 20 U of oxytocin in 1 L of Ringer’s solution.
**Outcome measures:** The amount of bleeding was assessed in both groups. Hemoglobin and hematocrit levels were measured in all the participants 6 h after childbirth. The statistical analysis of the data was performed in SPSS-17 using the following tests: independent t, paired t, repeated measures ANOVA, Friedman’s, Wilcoxon, Mann–Whitney, Fisher’s exact, and chi square. P-value <0.05 was considered statistically significant.

**Results:** There were no significant differences between groups in baseline characteristics (p > 0.05). After the intervention, there was significant decrease in the amount of postpartum bleeding in both groups. However, the mean decrease in the amount of bleeding was significantly more in the Capsella bursa pastoris group (p < 0.001).

**Conclusion:** Compared with the mere administration of oxytocin, sublingual Capsella bursa drops appear to be effective in reducing PPH in this study. Further research regarding the efficacy and safety of various doses of Capsella bursa pastoris is required.


**Abstract:**

**Background:** LDL cholesterol is a well established risk factor for atherosclerotic cardiovascular disease. How much one should or safely can lower this risk factor remains debated. We aimed to explore the relationship between progressively lower LDL-cholesterol concentrations achieved at 4 weeks and clinical efficacy and safety in the FOURIER trial of evolocumab, a monoclonal antibody to proprotein convertase subtilisin-kexin type 9 (PCSK9).

**Methods:** In this prespecified secondary analysis of 25 982 patients from the randomised FOURIER trial, the relationship between achieved LDL-cholesterol concentration at 4 weeks and subsequent cardiovascular outcomes (primary endpoint was the composite of cardiovascular death, myocardial infarction, stroke, coronary revascularisation, or unstable angina; key secondary endpoint was the composite of cardiovascular death, myocardial infarction, or stroke) and ten prespecified safety events of interest was examined over a median of 2.2 years of follow-up. We used multivariable modelling to adjust for baseline factors associated with achieved LDL cholesterol. This trial is registered with ClinicalTrials.gov, number NCT01764633.

**Findings:** Between Feb 8, 2013, and June 5, 2015, 27 564 patients were randomly assigned a treatment in the FOURIER study. 1025 (4%) patients did not have an LDL cholesterol measured at 4 weeks and 557 (2%) had already had a primary endpoint event or one of the ten prespecified safety events before the week-4 visit. From the remaining 25 982 patients (94% of those randomly assigned) 13013 were assigned evolocumab and 12 969 were assigned placebo. 2669 (10%) of 25982 patients achieved LDL-cholesterol concentrations of less than 0.5 mmol/L, 8003 (31%) patients achieved concentrations between 0.5 and less than 1.3 mmol/L, 3444 (13%) patients achieved concentrations between 1.3 and less than 1.8 mmol/L, 7471 (29%) patients achieved concentrations between 1.8 to less than 2.6 mmol/L, and 4395 (17%) patients achieved concentrations of 2.6 mmol/L or higher. There was a highly significant monotonic relationship between low LDL-cholesterol concentrations and lower risk of the primary and secondary efficacy composite endpoints extending to the bottom first percentile (LDL-cholesterol concentrations of less than 0.2 mmol/L; p=0.0012 for the primary endpoint, p=0.0001 for the secondary endpoint). Conversely, no significant association was observed between
achieved LDL cholesterol and safety outcomes, either for all serious adverse events or any of the other nine prespecified safety events.

**Interpretation:** There was a monotonic relationship between achieved LDL cholesterol and major cardiovascular outcomes down to LDL-cholesterol concentrations of less than 0.2 mmol/L. Conversely, there were no safety concerns with very low LDL-cholesterol concentrations over a median of 2.2 years. These data support further LDL-cholesterol lowering in patients with cardiovascular disease to well below current recommendations.


**Abstract:**

Polymyalgia rheumatica is an inflammatory disease that affects the shoulder, the pelvic girdles, and the neck, usually in individuals older than 50 years. Increases in acute phase reactants are typical of polymyalgia rheumatica. The disorder might present as an isolated condition or in association with giant cell arteritis. Several diseases, including inflammatory rheumatic and autoimmune diseases, infections, and malignancies can mimic polymyalgia rheumatica. Imaging techniques have identified the presence of bursitis in more than half of patients with active disease. Vascular uptake on PET scans is seen in some patients. A dose of 12.5–25.0 mg prednisolone daily or equivalent leads to rapid improvement of symptoms in most patients with isolated disease. However, relapses are common when prednisolone is tapered. Methotrexate might be used in patients who relapse. The effectiveness of biological therapies, such as anti-interleukin 6, in patients with polymyalgia rheumatica that is refractory to glucocorticoids requires further investigation. Most population-based studies indicate that mortality is not increased in patients with isolated disease.


**Abstract:**

**Objectives:** This study was planned to investigate the effect of a mixture of beeswax, olive oil and A. Tinctoria (L.) Tausch on burn wounds to determine the impact on burn healing, pain during dressing changes and duration of hospital stay.

**Methods:** The study was conducted between May 2014 and August 2015 in the Burn Unit of Ataturk University Research Hospital. The sample of this experimental study consisted of 64 patients (31 experimental group and 33 control group) who met its inclusion criteria. While the specially prepared dressing material was applied to the experimental group, the control group was administered the clinic’s routine dressing. The injuries were photographed before each dressing. Each picture was uploaded to a
computer for measurement with ImageJ software. Numbers, percentages, chi square, Independent samples t-test and Mann-Whitney U tests were used to assess the data.

**Results:** The patients in the experimental and control groups had similar descriptive characteristics and burn injury features (p > 0.05). The average age of the patients in the control group was $5.52 \pm 0.64$ years, and $6.68 \pm 1.09$ years in the experimental group. The majority of the patients were male (control: 54.5%, experimental: 58.1%). Boiling liquids were the most common cause of both groups’ burns (control: 93.9%, experiment: 83.9%). The most common first aid practice used was the application of cold water (control: 75.0%, experimental: 43.6%). The epithelization initiation time average of the experimental group patients (3.00 ± 0.85 days) was found to be earlier than that of the control group patients (6.90 ± 1.77 days), and this difference was statistically significant (p < 0.05). The mean pain scores experienced by the patients in the experimental group during dressing (8.12 ± 1.38) were determined to be lower than those of the control group (9.39 ± 1.05), and this difference was statistically significant (p < 0.05). It was also found that mean hospitalization durations of the patients in the experimental group (8.22 ± 3.05) were shorter than those of the control group (14.42 ± 7.79), and this difference was also found to be statistically significant (p < 0.05).

**Conclusion:** When a beeswax, olive oil and A. tinctoria (L.) Tausch mixture was applied to second degree burns, this accelerated epithelization, reduced the pain experienced during dressing changes and shortened the hospital stay durations of the patients.


**Abstract:**

**Background:** This paper examines a paradox in the German healthcare system: Complementary and alternative medicine (CAM) practices are a major element of medical encounters in Germany. Patients seek them, physicians provide them, and public health insurances pay for them in part. Despite all this, CAM practices are not acknowledged as scientifically valid.

**Material and Method:** I will examine this situation in detail based on 2 ethnographic studies. The first study refers to an attempt to introduce homeopathic education at a German university. The second one is a study in the context of cancer and CAM. These cases are perfect examples of the current power struggles that are impeding the expansion of CAM practices in Germany.

**Results:** The results should be seen from the theoretical angle of the study of science. The conventional method of proving scientific validity is in contradiction to those
frameworks in which the impact of CAM might be demonstrated. There are economic interests invested in preventing the integration of CAM into existing scientific structures. However, the current hybridization of CAM with conventional medicine might be a step towards an institutionalized heterogenization of medical practices in Germany.

**Conclusions:** A broader understanding of scientific methods within the CAM community could provide a useful frame for future research. I suggest that the CAM community more actively takes part in the discourse with representatives of conventional medicine and come out of the closet.


**Abstract:**

Transportation-related risk factors are a major source of morbidity and mortality in China, where the expansion of road networks and surges in personal vehicle ownership are having profound effects on public health. Road traffic injuries and fatalities have increased alongside increased use of motorised transport in China, and accident injury risk is aggravated by inadequate emergency response systems and trauma care. National air quality standards and emission control technologies are having a positive effect on air quality, but persistent air pollution is increasingly attributable to a growing and outdated vehicle fleet and to famously congested roads. Urban design favours motorised transport, and physical activity and its associated health benefits are hindered by poor urban infrastructure. Transport emissions of greenhouse gases contribute substantially to regional and global climate change, which compound public health risks from multiple factors. Despite these complex challenges, technological advances and innovations in planning and policy stand to make China a leader in sustainable, healthy transportation.


**Abstract:**

**Background:** Little is known about how the proportions of dependency states have changed between generational cohorts of older people. We aimed to estimate years lived in different dependency states at age 65 years in 1991 and 2011, and new projections of future demand for care.

**Methods:** In this population-based study, we compared two Cognitive Function and Ageing Studies (CFAS I and CFAS II) of older people (aged ≥65 years) who were permanently registered with a general practice in three defined geographical areas (Cambridgeshire, Newcastle, and Nottingham; UK). These studies were done two decades apart (1991 and 2011). General practices provided lists of individuals to be contacted and were asked to exclude those who had died or might die over the next month. Baseline interviews were done in the community and care homes. Participants were stratified by age, and interviews occurred only after written informed consent was obtained. Information collected included basic sociodemographics, cognitive status, urinary incontinence, and self-reported ability to do activities of daily living. CFAS I was assigned as the 1991 cohort and CFAS II as the 2011 cohort, and both studies provided prevalence estimates of dependency in four states: high dependency (24-h care), medium dependency (daily care), low dependency (less than daily), and independent. Years in each dependency
state were calculated by Sullivan’s method. To project future demands for social care, the proportions in each dependency state (by age group and sex) were applied to the 2014 England population projections.

**Findings:** Between 1991 and 2011, there were significant increases in years lived from age 65 years with low dependency (1.7 years [95% CI 1.0–2.4] for men and 2.4 years [1.8–3.1] for women) and increases with high dependency (0.9 years [0.2–1.7] for men and 1.3 years [0.5–2.1] for women). The majority of men’s extra years of life were spent independent (36.3%) or with low dependency (36.3%) whereas for women the majority were spent with low dependency (58.0%), and only 4.8% were independent. There were substantial reductions in the proportions with medium and high dependency who lived in care homes, although, if these dependency and care home proportions remain constant in the future, further population ageing will require an extra 712,15 care home places by 2025.

**Interpretation:** On average older men now spend 2.4 years and women 3.0 years with substantial care needs, and most will live in the community. These findings have considerable implications for families of older people who provide the majority of unpaid care, but the findings also provide valuable new information for governments and care providers planning the resources and funding required for the care of their future ageing populations.

**Funding:** Medical Research Council (G9901400) and (G06010220), with support from the National Institute for Health Research Comprehensive Local research networks in West Anglia and Trent, UK, and Neurodegenerative Disease Research Network in Newcastle, UK.


**Abstract:**

Atrial fibrillation is one of the major cardiovascular health problems: it is a common, chronic condition, affecting 2–3% of the population in Europe and the USA and requiring 1–3% of health-care expenditure as a result of stroke, sudden death, heart failure, unplanned hospital admissions, and other complications. Early diagnosis of atrial fibrillation, ideally before the first complication occurs, remains a challenge, as shown by patients who are only diagnosed with the condition when admitted to hospital for acute cardiac decompensation or stroke. Once diagnosed, atrial fibrillation requires chronic, multidimensional management in five domains (acute management, treatment of underlying and concomitant cardiovascular conditions, stroke prevention therapy, rate control, and rhythm control). The consistent provision of these treatment options to all patients with atrial fibrillation is difficult, despite recent improvements in organisation of care, knowledge about atrial fibrillation, and treatment options. Integrated care models that provide patient-centred care in, or close to, the patient’s community while maintaining access to all specialist treatment options, emerge as the best approach to achieve consistent delivery of these chronic treatments to all patients with atrial fibrillation. Ongoing research efforts will establish when to initiate oral anticoagulation in patients with device-detected atrial high-rate episodes, quantify the prognostic effect of early and comprehensive rhythm control therapy, including atrial fibrillation ablation, and delineate optimum methods to reduce bleeding complications in patients treated with anticoagulation. Additionally, research efforts are needed to define different types of atrial
fibrillation on the basis of the main causes of atrial fibrillation to pave the way for the clinical development of stratified atrial fibrillation therapy.

**Langdahl Bente L, Libanati Cesar, Crittenden Daria B et al. Romosozumab (sclerostin monoclonal antibody) versus teriparatide in postmenopausal women with osteoporosis transitioning from oral bisphosphonate therapy: A randomised, open-label, phase 3 trial. Lancet 2017; 390(10102): 1585-94p.**

**Abstract:**

**Background:** Previous bisphosphonate treatment attenuates the bone-forming effect of teriparatide. We compared the effects of 12 months of romosozumab (AMG 785), a sclerostin monoclonal antibody, versus teriparatide on bone mineral density (BMD) in women with postmenopausal osteoporosis transitioning from bisphosphonate therapy.

**Methods:** This randomised, phase 3, open-label, active-controlled study was done at 46 sites in North America, Latin America, and Europe. We enrolled women (aged ≥55 to ≤90 years) with postmenopausal osteoporosis who had taken an oral bisphosphonate for at least 3 years before screening and alendronate the year before screening; an areal BMD T score of −2·5 or lower at the total hip, femoral neck, or lumbar spine; and a history of fracture. Patients were randomly assigned (1:1) via an interactive voice response system to receive subcutaneous romosozumab (210 mg once monthly) or subcutaneous teriparatide (20 μg once daily). The primary endpoint was percentage change from baseline in areal BMD by dual-energy x-ray absorptiometry at the total hip through month 12 (mean of months 6 and 12), which used a linear mixed effects model for repeated measures and represented the mean treatment effect at months 6 and 12. All randomised patients with a baseline measurement and at least one post-baseline measurement were included in the efficacy analysis. This trial is registered with ClinicalTrials.gov, number NCT01796301.

**Findings:** Between Jan 31, 2013, and April 29, 2014, 436 patients were randomly assigned to romosozumab (n=218) or teriparatide (n=218). 206 patients in the romosozumab group and 209 in the teriparatide group were included in the primary efficacy analysis. Through 12 months, the mean percentage change from baseline in total hip areal BMD was 2·6% (95% CI 2·2 to 3·0) in the romosozumab group and −0·6% (−1·0 to −0·2) in the teriparatide group; difference 3·2% (95% CI 2·7 to 3·8; p<0·0001). The frequency of adverse events was generally balanced between treatment groups. The most frequently reported adverse events were nasopharyngitis (28 [13%] of 218 in the romosozumab group vs 22 [10%] of 214 in the teriparatide group), hypercalcaemia (two [<1%] vs 22 [10%]), and arthralgia (22 [10%] vs 13 [6%]). Serious adverse events were reported in 17 (8%) patients on romosozumab and in 23 (11%) on teriparatide; none were judged treatment related. There were six (3%) patients in the romosozumab group compared with 12 (6%) in the teriparatide group with adverse events leading to investigational product withdrawal.

**Interpretation:** Transition to a bone-forming agent is common practice in patients treated with bisphosphonates, such as those who fracture while on therapy. In such patients, romosozumab led to gains in hip BMD that were not observed with teriparatide. These data could inform clinical decisions for patients at high risk of fracture.

**Funding:** Amgen, Astellas, and UCB Pharma.

**Abstract:**

The global nephrology community recognises the need for a cohesive plan to address the problem of chronic kidney disease (CKD). In July, 2016, the International Society of Nephrology hosted a CKD summit of more than 85 people with diverse expertise and professional backgrounds from around the globe. The purpose was to identify and prioritise key activities for the next 5–10 years in the domains of clinical care, research, and advocacy and to create an action plan and performance framework based on ten themes: strengthen CKD surveillance; tackle major risk factors for CKD; reduce acute kidney injury—a special risk factor for CKD; enhance understanding of the genetic causes of CKD; establish better diagnostic methods in CKD; improve understanding of the natural course of CKD; assess and implement established treatment options in patients with CKD; improve management of symptoms and complications of CKD; develop novel therapeutic interventions to slow CKD progression and reduce CKD complications; and increase the quantity and quality of clinical trials in CKD. Each group produced a prioritised list of goals, activities, and a set of key deliverable objectives for each of the themes. The intended users of this action plan are clinicians, patients, scientists, industry partners, governments, and advocacy organisations. Implementation of this integrated comprehensive plan will benefit people who are at risk for or affected by CKD worldwide.


**Abstract:**

**Background:** Total glucosides of paeony (TGP) is commonly used to treat rheumatoid arthritis (RA) in China. However, clinical practice hasn’t been well informed by evidence from appropriately conducted systematic reviews. This PRISMA-compliant systematic review aims at examining the effectiveness and safety of TGP for RA.

**Methods:** Randomized controlled trials (RCTs) comparing TGP with placebo, no treatment, or disease-modifying antirheumatic drugs (DMARDs) for patients with RA were retrieved by searching seven databases. Primary outcomes included disease improvement and disease remission. Secondary outcomes included adverse effects, pain, health-related quality of life, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Data extraction and analyses were conducted according to the Cochrane standards. We assessed risk of bias for each included studies and quality of evidence on pre-specified outcomes.

**Results:** Eight studies enrolling 1209 patients with active RA were included in this systematic review. On the basis of traditional DMARD(s), TGP might be beneficial for patients with RA in improvement of American College of Rheumatology (ACR) 20 response rate, ACR 50 response rate, ACR70 response rate, and in reduction of adverse effects, compared with no treatment. The overall methodological quality of included studies and the quality of evidence for each outcome were limited.

**Conclusions:** Current trials suggested potential benefits of TGP for RA on the basis of traditional DMARD(s). Therefore, TGP may be a good choice for RA as an adjuvant
therapy. However, considering the limited methodological quality and strength of evidence, high-quality RCTs are warranted to support the use of TGP for RA.


**Abstract:**

**Background:** Niemann-Pick disease, type C1 (NPC1) is a lysosomal storage disorder characterised by progressive neurodegeneration. In preclinical testing, 2-hydroxypropyl-β-cyclodextrins (HPβCD) significantly delayed cerebellar Purkinje cell loss, slowed progression of neurological manifestations, and increased lifespan in mouse and cat models of NPC1. The aim of this study was to assess the safety and efficacy of lumbar intrathecal HPβCD.

**Methods:** In this open-label, dose-escalation phase 1–2a study, we gave monthly intrathecal HPβCD to participants with NPC1 with neurological manifestation at the National Institutes of Health (NIH), Bethesda, MD, USA. To explore the potential effect of 2-week dosing, three additional participants were enrolled in a parallel study at Rush University Medical Center (RUMC), Chicago, IL, USA. Participants from the NIH were non-randomly, sequentially assigned in cohorts of three to receive monthly initial intrathecal HPβCD at doses of 50, 200, 300, or 400 mg per month. A fifth cohort of two participants received initial doses of 900 mg. Participants from RUMC initially received 200 or 400 mg every 2 weeks. The dose was escalated based on intolerance or safety data from higher dose cohorts. Serum and CSF 24(S)-hydroxycholesterol (24[S]-HC), which serves as a biomarker of target engagement, and CSF protein biomarkers were evaluated. NPC Neurological Severity Scores (NNSS) were used to compare disease progression in HPβCD-treated participants relative to a historical comparison cohort of 21 NPC1 participants of similar age range.

**Findings:** Between Sept 21, 2013, and Jan 19, 2015, 32 participants with NPC1 were assessed for eligibility at the National Institutes of Health. 18 patients were excluded due to inclusion criteria not met (six patients), declined to participate (three patients), pursued independent expanded access and obtained the drug outside of the study (three patients), enrolled in the RUMC cohort (one patient), or too late for the trial enrolment (five patients). 14 patients were enrolled and sequentially assigned to receive intrathecal HPβCD at a starting dose of 50 mg per month (three patients), 200 mg per month (three patients), 300 mg per month (three patients), 400 mg per month (three patients), or 900 mg per month (two patients). During the first year, two patients had treatment interrupted for one dose, based on grade 1 ototoxicity. All 14 patients were assessed at 12 months. Between 12 and 18 months, one participant had treatment interrupted at 17 months due to hepatocellular carcinoma, one patient had dose interruption for 2 doses based on caregiver hardship and one patient had treatment interrupted for 1 dose for mastoiditis. 11 patients were assessed at 18 months. Between Dec 11, 2013, and June 25, 2014, three participants were assessed for eligibility and enrolled at RUMC, and were
assigned to receive intrathecal HPβCD at a starting dose of 200 mg every 2 weeks (two patients), or 400 mg every two weeks (one patient). There were no dropouts in this group and all 3 patients were assessed at 18 months. Biomarker studies were consistent with improved neuronal cholesterol homoeostasis and decreased neuronal pathology. Post-drug plasma 24(S)-HC area under the curve (AUC8-72) values, an indicator of neuronal cholesterol homoeostasis, were significantly higher than post-saline plasma 24(S)-HC AUC8-72 after doses of 900 mg (p=0.0063) and 1200 mg (p=0.0037). CSF 24(S)-HC concentrations in three participants given either 600 or 900 mg of HPβCD were increased about two fold (p=0.0032) after drug administration. No drug-related serious adverse events were observed. Mid-frequency to high-frequency hearing loss, an expected adverse event, was documented in all participants. When managed with hearing aids, this did not have an appreciable effect on daily communication. The NNSS for the 14 participants treated monthly increased at a rate of 1.22, SEM 0.34 points per year compared with 2.92, SEM 0.27 points per year (p=0.0002) for the 21 patient comparison group. Decreased progression was observed for NNSS domains of ambulation (p=0.0622), cognition (p=0.0040) and speech (p=0.0423).

**Interpretation:** Patients with NPC1 treated with intrathecal HPβCD had slowed disease progression with an acceptable safety profile. These data support the initiation of a multinational, randomised, controlled trial of intrathecal HPβCD.

**Funding:** National Institutes of Health, Dana’s Angels Research Trust, Ara Parseghian Medical Research Foundation, Hope for Haley, Samantha’s Search for the Cure Foundation, National Niemann-Pick Disease Foundation, Support of Accelerated Research for NPC Disease, Vtesse, Janssen Research and Development, a Johnson & Johnson company, and Johnson & Johnson.


**Abstract:**

**Objectives:** The incorporation of certain alkalinizing vegetables, fruits, milk and its products in the diet has been known to alleviate hyperacidity. These foods help to restore the natural gastric balance and function, curb acid reflux, aid digestion, reduce the burning sensation due to hyperacidity and soothe the inflamed mucosa of the stomach. The present study evaluates and compares the antacid effect of broccoli, kale, radish, cucumber, lemon juice, cold milk and curd in an artificial stomach model.

**Design:** The pH of the test samples and their neutralizing effect on artificial gastric acid was determined and compared with that of water, the active control sodium bicarbonate and a marketed antacid preparation ENO. A modified model of Vatier’s artificial stomach was used to determine the duration of consistent neutralization of artificial gastric acid by the test samples. The neutralizing capacity of the test samples was determined in vitro using the classical titration method of Fordtran.

**Results:** All test samples except lemon showed significantly higher (p < 0.05 for cucumber and p < 0.001 for the rest) acid neutralizing effect than water. All test samples also exhibited a significantly (p < 0.001) higher duration of consistent neutralization and higher antacid capacity than water. Highest antacid activity was demonstrated by cold milk and broccoli which was comparable with ENO and sodium bicarbonate.
Conclusion: It may be concluded that the natural food ingredients used in this study exhibited significant antacid activity, justifying their use as essential dietary components to counter hyperacidity.


Abstract:

Background: Agricultural pesticide self-poisoning is a major public health problem in rural Asia. The use of safer household pesticide storage has been promoted to prevent deaths, but there is no evidence of effectiveness. We aimed to test the effectiveness of lockable household containers for prevention of pesticide self-poisoning.

Methods: We did a community-based, cluster-randomised controlled trial in a rural area of North Central Province, Sri Lanka. Clusters of households were randomly assigned (1:1), with a sequence computer-generated by a minimisation process, to intervention or usual practice (control) groups. Intervention households that had farmed or had used or stored pesticide in the preceding agricultural season were given a lockable storage container. Further promotion of use of the containers was restricted to community posters and 6-monthly reminders during routine community meetings. The primary outcome was incidence of pesticide self-poisoning in people aged 14 years or older during 3 years of follow-up. Identification of outcome events was done by staff who were unaware of group allocation. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT1146496.

Findings: Between Dec 31, 2010, and Feb 2, 2013, we randomly assigned 90 rural villages to the intervention group and 90 to the control group. 27 091 households (114 168 individuals) in the intervention group and 26 291 households (109 693 individuals) in the control group consented to participate. 20 457 household pesticide storage containers were distributed. In individuals aged 14 years or older, 611 cases of pesticide self-poisoning had occurred by 3 years in the intervention group compared with 641 cases in the control group; incidence of pesticide self-poisoning did not differ between groups (293·3 per 100 000 person-years of follow-up in the intervention group vs 318·0 per 100 000 in the control group; rate ratio [RR] 0·93, 95% CI 0·80–1·08; p=0·33). We found no evidence of switching from pesticide self-poisoning to other forms of self-harm, with no significant difference in the number of fatal (82 in the intervention group vs 67 in the control group; RR 1·22, 0·88–1·68) or non-fatal (1135 vs 1153; RR 0·97, 0·86–1·08) self-harm events involving all methods.

Interpretation: We found no evidence that means reduction through improved household pesticide storage reduces pesticide self-poisoning. Other approaches, particularly removal of highly hazardous pesticides from agricultural practice, are likely to be more effective for suicide prevention in rural Asia.


Abstract:
**Background:** Gonorrhoea is a major global public health problem that is exacerbated by drug resistance. Effective vaccine development has been unsuccessful, but surveillance data suggest that outer membrane vesicle meningococcal group B vaccines affect the incidence of gonorrhoea. We assessed vaccine effectiveness of the outer membrane vesicle meningococcal B vaccine (MeNZB) against gonorrhoea in young adults aged 15–30 years in New Zealand.

**Methods:** We did a retrospective case-control study of patients at sexual health clinics aged 15–30 years who were born between Jan 1, 1984, and Dec 31, 1998, eligible to receive MeNZB, and diagnosed with gonorrhoea or chlamydia, or both. Demographic data, sexual health clinic data, and National Immunisation Register data were linked via patients’ unique personal identifier. For primary analysis, cases were confirmed by laboratory isolation or detection of Neisseria gonorrhoeae only from a clinical specimen, and controls were individuals with a positive chlamydia test only. We estimated odds ratios (ORs) comparing disease outcomes in vaccinated versus unvaccinated participants via multivariable logistic regression. Vaccine effectiveness was calculated as 100×(1–OR).

**Findings:** 11 of 24 clinics nationally provided records. There were 14 730 cases and controls for analyses: 1241 incidences of gonorrhoea, 12 487 incidences of chlamydia, and 1002 incidences of co-infection. Vaccinated individuals were significantly less likely to be cases than controls (511 [41%] vs 6424 [51%]; adjusted OR 0·69 [95% CI 0·61–0·79]; p<0·0001). Estimate vaccine effectiveness of MeNZB against gonorrhoea after adjustment for ethnicity, deprivation, geographical area, and sex was 31% (95% CI 21–39).

**Interpretation:** Exposure to MeNZB was associated with reduced rates of gonorrhoea diagnosis, the first time a vaccine has shown any protection against gonorrhoea. These results provide a proof of principle that can inform prospective vaccine development not only for gonorrhoea but also for meningococcal vaccines.

**Funding:** GSK Vaccines.


**Abstract:**

**Background:** Inflammation in the tumour microenvironment mediated by interleukin 1β is hypothesised to have a major role in cancer invasiveness, progression, and metastases. We did an additional analysis in the Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS), a randomised trial of the role of interleukin-1β inhibition in atherosclerosis, with the aim of establishing whether inhibition of a major product of the Nod-like receptor protein 3 (NLRP3) inflammasome with canakinumab might alter cancer incidence.
Methods: We did a randomised, double-blind, placebo-controlled trial of canakinumab in 10 061 patients with atherosclerosis who had had a myocardial infarction, were free of previously diagnosed cancer, and had concentrations of high-sensitivity C-reactive protein (hsCRP) of 2 mg/L or greater. To assess dose–response effects, patients were randomly assigned by computer-generated codes to three canakinumab doses (50 mg, 150 mg, and 300 mg, subcutaneously every 3 months) or placebo. Participants were followed up for incident cancer diagnoses, which were adjudicated by an oncology endpoint committee masked to drug or dose allocation. Analysis was by intention to treat. The trial is registered with ClinicalTrials.gov, NCT01327846. The trial is closed (the last patient visit was in June, 2017).

Findings: Baseline concentrations of hsCRP (median 6·0 mg/L vs 4·2 mg/L; p<0·0001) and interleukin 6 (3·2 vs 2·6 ng/L; p<0·0001) were significantly higher among participants subsequently diagnosed with lung cancer than among those not diagnosed with cancer. During median follow-up of 3·7 years, compared with placebo, canakinumab was associated with dose-dependent reductions in concentrations of hsCRP of 26–41% and of interleukin 6 of 25–43% (p<0·0001 for all comparisons). Total cancer mortality (n=196) was significantly lower in the pooled canakinumab group than in the placebo group (p=0·0007 for trend across groups), but was significantly lower than placebo only in the 300 mg group individually (hazard ratio [HR] 0·49 [95% CI 0·31–0·75]; p=0·0009). Incident lung cancer (n=129) was significantly less frequent in the canakinumab 300 mg group than in the placebo group (HR 0·61 [95% CI 0·39–0·97]; p=0·034) and in the 300 mg groups (HR 0·33 [95% CI 0·18–0·59]; p<0·0001; p<0·0001 for trend across groups). Lung cancer mortality was significantly less common in the canakinumab 300 mg group than in the placebo group (HR 0·23 [95% CI 0·10–0·54]; p=0·0002) and in the pooled canakinumab population than in the placebo group (p=0·0002 for trend across groups). Fatal infections or sepsis were significantly more common in the canakinumab groups than in the placebo group. All-cause mortality did not differ significantly between the canakinumab and placebo groups (HR 0·94 [95% CI 0·83–1·06]; p=0·31).

Interpretation: Our hypothesis-generating data suggest the possibility that anti-inflammatory therapy with canakinumab targeting the interleukin-1β innate immunity pathway could significantly reduce incident lung cancer and lung cancer mortality. Replication of these data in formal settings of cancer screening and treatment is required.


Abstract:

Background: Hereditary angio-oedema is a recurrent, oedematous disorder caused by deficiency of functional C1 inhibitor. Infusions of plasma-derived C1 esterase inhibitor deter attacks of hereditary angio-oedema, but the prophylactic effect of recombinant human C1 esterase inhibitor has not been rigorously studied. We aimed to assess the efficacy of recombinant human C1 esterase inhibitor for prophylaxis of hereditary angio-oedema.

Methods: We conducted this phase 2, multicentre, randomised, double-blind, placebo-controlled crossover trial at ten centres in Canada, the Czech Republic, Israel, Italy, Macedonia, Romania, Serbia, and the USA. We enrolled patients aged 13 years or older with functional C1-inhibitor concentrations of less than 50% of normal and a history of
four or more attacks of hereditary angio-oedema per month for at least 3 months before study initiation. Patients were randomly assigned centrally (1:1:1:1:1:1), via an interactive response technology system with fixed allocation, to receive one of six treatment sequences. During each sequence, patients received intravenous recombinant human C1 esterase inhibitor (50 IU/kg; maximum 4200 IU) twice weekly, recombinant human C1 esterase inhibitor once weekly and placebo once weekly, and placebo twice weekly, each for 4 weeks with a 1 week washout period between crossover. All patients, investigators, and study personnel who participated in patient care were masked to group allocation during the study. The primary efficacy endpoint was the number of attacks of hereditary angio-oedema observed in each 4 week treatment period. Attack symptoms were recorded daily. The primary efficacy analysis was done in the intention-to-treat population. Safety was assessed in all patients who received at least one injection of study medication. This study is registered with ClinicalTrials.gov, number NCT02247739.

Findings: Between Dec 29, 2014, and May 3, 2016, we enrolled 35 patients, of whom 32 (91%) underwent randomisation (intention-to-treat population) and 26 (81%) completed the study. The mean number of attacks of hereditary angio-oedema over 4 weeks was significantly reduced with recombinant human C1 esterase inhibitor twice weekly (2·7 attacks [SD 2·4]) and once weekly (4·4 attacks [3·2]) versus placebo (7·2 attacks [3·6]), with mean differences of −4·4 attacks (p<0·0001) and −2·8 attacks (p=0·0004), respectively. We recorded adverse events in ten (34%) of 29 patients given twice-weekly recombinant human C1 esterase inhibitor, 13 (45%) of 29 patients given the once-weekly regimen, and eight (29%) of 28 patients given placebo. Headache (twice-weekly treatment) and nasopharyngitis (once-weekly treatment) were the most common adverse events. Two (7%) adverse events (fatigue and headache) were deemed possibly related to treatment with recombinant human C1 esterase inhibitor, but both resolved without additional treatment. No thrombotic or thromboembolic events, systemic allergic reactions (including anaphylaxis), or neutralising antibodies were reported.

Interpretation: Prophylaxis with recombinant human C1 esterase inhibitor provided clinically relevant reductions in frequency of hereditary angio-oedema attacks and was well tolerated. In view of the pharmacokinetic profile of recombinant human C1 esterase inhibitor, our results suggest that efficacy of C1-inhibitor replacement therapy might not be a direct function of plasma trough concentrations of C1 inhibitor.

Funding: Pharming Technologies.


Abstract:

Background: Interim analyses of the phase 3 KEYNOTE-006 study showed superior overall and progression-free survival of pembrolizumab versus ipilimumab in patients with advanced melanoma. We present the final protocol-specified survival analysis.

Methods: In this multicentre, open-label, randomised, phase 3 trial, we recruited patients from 87 academic institutions, hospitals, and cancer centres in 16 countries (Australia, Austria, Belgium, Canada, Chile, Colombia, France, Germany, Israel, Netherlands, New Zealand, Norway, Spain, Sweden, UK, and USA). We randomly assigned
participants (1:1:1) to one of two dose regimens of pembrolizumab, or one regimen of ipilimumab, using a centralised, computer-generated allocation schedule. Treatment assignments used blocked randomisation within strata. Eligible patients were at least 18 years old, with an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, at least one measurable lesion per Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST v1.1), unresectable stage III or IV melanoma (excluding ocular melanoma), and up to one previous systemic therapy (excluding anti-CTLA-4, PD-1, or PD-L1 agents). Secondary eligibility criteria are described later. Patients were excluded if they had active brain metastases or active autoimmune disease requiring systemic steroids. The primary outcome was overall survival (defined as the time from randomisation to death from any cause). Response was assessed per RECIST v1.1 by independent central review at week 12, then every 6 weeks up to week 48, and then every 12 weeks thereafter. Survival was assessed every 12 weeks, and final analysis occurred after all patients were followed up for at least 21 months. Primary analysis was done on the intention-to-treat population (all randomly assigned patients) and safety analyses were done in the treated population (all randomly assigned patients who received at least one dose of study treatment). Data cutoff date for this analysis was Dec 3, 2015. This study was registered with ClinicalTrials.gov, number NCT01866319.

Findings: Between Sept 18, 2013, and March 3, 2014, 834 patients with advanced melanoma were enrolled and randomly assigned to receive intravenous pembrolizumab every 2 weeks (n=279), intravenous pembrolizumab every 3 weeks (n=277), or intravenous ipilimumab every 3 weeks (ipilimumab for four doses; n=278). One patient in the pembrolizumab 2 week group and 22 patients in the ipilimumab group withdrew consent and did not receive treatment. A total of 811 patients received at least one dose of study treatment. Median follow-up was 22·9 months; 383 patients died. Median overall survival was not reached in either pembrolizumab group and was 16·0 months with ipilimumab (hazard ratio [HR] 0·68, 95% CI 0·53–0·87 for pembrolizumab every 2 weeks vs ipilimumab; p=0·0009 and 0·68, 0·53–0·86 for pembrolizumab every 3 weeks vs ipilimumab; p=0·0008). 24-month overall survival rate was 55% in the 2-week group, 55% in the 3-week group, and 43% in the ipilimumab group.

Interpretation: Substantiating the results of the interim analyses of KEYNOTE-006, pembrolizumab continued to provide superior overall survival versus ipilimumab, with no difference between pembrolizumab dosing schedules. These conclusions further support the use of pembrolizumab as a standard of care for advanced melanoma.


Abstract:

Introduction: Migraine is a common and disabling primary headache disorder. Cupping is a traditional medical treatment used in several societies in East Asia and it is frequently used for controlling pain including migraine. There have been no systematic reviews on the treatment effects of cupping on migraine. Furthermore, related studies have had many limitations, making it unclear whether cupping intervention is beneficial for migraine. We propose to conduct a systematic review and meta-analysis to consider the evidence related to the effect of cupping on migraine.

Methods: We developed a protocol describing the essential reporting items based on the PRISMA for systematic review protocols 2015 (PRISMA-P 2015) (Registration number:
We will search eight databases and include data from prospective randomized controlled clinical trials or quasi-randomized controlled trials that used cupping interventions for the treatment of migraine. The risk of bias will be assessed with the “Risk of bias” tool from the Cochrane Handbook. Using improved effectiveness and the change in headache pain intensity as graded on the visual analogue scale as the primary outcomes, we will compare these outcomes between the cupping intervention and control groups.

**Conclusion:** There have been no systematic reviews of cupping therapy for migraine headaches to date. This systematic review will assess the effectiveness and safety of cupping therapy for migraine. This systematic review will inform and help healthcare practitioners to treat migraine and will be disseminated electronically and in print in a peer-reviewed journal.


**Abstract:**

Investment in the capabilities of the world’s 1·2 billion adolescents is vital to the UN’s Sustainable Development Agenda. We examined investments in countries of low income, lower-middle income, and upper-middle income covering the majority of these adolescents globally to derive estimates of investment returns given existing knowledge. The costs and effects of the interventions were estimated by adapting existing models and by extending methods to create new modelling tools. Benefits were valued in terms of increased gross domestic product and averted social costs. The initial analysis showed high returns for the modelled interventions, with substantial variation between countries and with returns generally higher in low-income countries than in countries of lower-middle and upper-middle income. For interventions targeting physical, mental, and sexual health (including a human papilloma virus programme), an investment of US$4·6 per capita each year from 2015 to 2030 had an unweighted mean benefit to cost ratio (BCR) of more than 10·0, whereas, for interventions targeting road traffic injuries, a BCR of 5·9 (95% CI 5·8–6·0) was achieved on investment of $0·6 per capita each year. Interventions to reduce child marriage ($3·8 per capita each year) had a mean BCR of 5·7 (95% CI 5·3–6·1), with the effect high in low-income countries. Investment to increase the extent and quality of secondary schooling is vital but will be more expensive than other interventions—investment of $22·6 per capita each year from 2015 to 2030 generated a mean BCR of 11·8 (95% CI 11·6–12·0). Investments in health and education will not only transform the lives of adolescents in resource-poor settings, but will also generate high economic and social returns. These returns were robust to substantial variation in assumptions. Although the knowledge base on the impacts of interventions is limited in many areas, and a major research effort is needed to build a more complete investment framework, these analyses suggest that comprehensive investments in adolescent health and wellbeing should be given high priority in national and international policy.


**Sibbing Dirk, Aradi Daniel, Jacobshagen Claudius et al. Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing**
Abstract:

Background: Current guidelines recommend potent platelet inhibition with prasugrel or ticagrelor for 12 months after an acute coronary syndrome managed with percutaneous coronary intervention (PCI). However, the greatest anti-ischaemic benefit of potent antiplatelet drugs over the less potent clopidogrel occurs early, while most excess bleeding events arise during chronic treatment. Hence, a stage-adapted treatment with potent platelet inhibition in the acute phase and de-escalation to clopidogrel in the maintenance phase could be an alternative approach. We aimed to investigate the safety and efficacy of early de-escalation of antiplatelet treatment from prasugrel to clopidogrel guided by platelet function testing (PFT).

Methods: In this investigator-initiated, randomised, open-label, assessor-blinded, multicentre trial (TROPICAL-ACS) done at 33 sites in Europe, patients were enrolled if they had biomarker-positive acute coronary syndrome with successful PCI and a planned duration of dual antiplatelet treatment of 12 months. Enrolled patients were randomly assigned (1:1) using an internet-based randomisation procedure with a computer-generated block randomisation with stratification across study sites to either standard treatment with prasugrel for 12 months (control group) or a step-down regimen (1 week prasugrel followed by 1 week clopidogrel and PFT-guided maintenance therapy with clopidogrel or prasugrel from day 14 after hospital discharge; guided de-escalation group). The assessors were masked to the treatment allocation. The primary endpoint was net clinical benefit (cardiovascular death, myocardial infarction, stroke or bleeding grade 2 or higher according to Bleeding Academic Research Consortium [BARC] criteria) 1 year after randomisation (non-inferiority hypothesis; margin of 30%). Analysis was intention to treat. This study is registered with ClinicalTrials.gov, number NCT01959451, and EudraCT, 2013-001636-22.

Findings: Between Dec 2, 2013, and May 20, 2016, 2610 patients were assigned to study groups; 1304 to the guided de-escalation group and 1306 to the control group. The primary endpoint occurred in 95 patients (7%) in the guided de-escalation group and in 118 patients (9%) in the control group (pnon-inferiority=0·0004; hazard ratio [HR] 0·81 [95% CI 0·62–1·06], psuperiority=0·12). Despite early de-escalation, there was no increase in the combined risk of cardiovascular death, myocardial infarction, or stroke in the de-escalation group (32 patients [3%]) versus in the control group (42 patients [3%]; pnon-inferiority=0·0115). There were 64 BARC 2 or higher bleeding events (5%) in the de-escalation group versus 79 events (6%) in the control group (HR 0·82 [95% CI 0·59–1·13]; p=0·23).

Interpretation: Guided de-escalation of antiplatelet treatment was non-inferior to standard treatment with prasugrel at 1 year after PCI in terms of net clinical benefit. Our trial shows that early de-escalation of antiplatelet treatment can be considered as an alternative approach in patients with acute coronary syndrome managed with PCI.

Funding: Klinikum der Universität München, Roche Diagnostics, Eli Lilly, and Daiichi Sankyo.

Abstract:

**Background:** The development of coronary drug-eluting stents has included use of new metal alloys, changes in stent architecture, and use of bioresorbable polymers. Whether these advancements improve clinical safety and efficacy has not been shown in previous randomised trials. We aimed to examine the clinical outcomes of a bioresorbable polymer sirolimus-eluting stent compared with a durable polymer everolimus-eluting stent in a broad patient population undergoing percutaneous coronary intervention.

**Methods:** BIOFLOW V was an international, randomised trial done in patients undergoing elective and urgent percutaneous coronary intervention in 90 hospitals in 13 countries (Australia, Belgium, Canada, Denmark, Germany, Hungary, Israel, the Netherlands, New Zealand, South Korea, Spain, Switzerland, and the USA). Eligible patients were those aged 18 years or older with ischaemic heart disease undergoing planned stent implantation in de-novo, native coronary lesions. Patients were randomly assigned (2:1) to either an ultrathin strut (60 μm) bioresorbable polymer sirolimus-eluting stent or to a durable polymer everolimus-eluting stent. Randomisation was via a central web-based data capture system (mixed blocks of 3 and 6), and stratified by study site. The primary endpoint was 12-month target lesion failure. The primary non-inferiority comparison combined these data from two additional randomised trials of bioresorbable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent with Bayesian methods. Analysis was by intention to treat. The trial is registered with ClinicalTrials.gov, number NCT02389946.

**Findings:** Between May 8, 2015, and March 31, 2016, 4772 patients were recruited into the study. 1334 patients met inclusion criteria and were randomly assigned to treatment with bioresorbable polymer sirolimus-eluting stents (n=884) or durable polymer everolimus-eluting stents (n=450). 52 (6%) of 883 patients in the bioresorbable polymer sirolimus-eluting stent group and 41 (10%) of 427 patients in the durable polymer everolimus-eluting stent group met the 12-month primary endpoint of target lesion failure (95% CI −6·84 to −0·29, p=0·0399), with differences in target vessel myocardial infarction (39 [5%] of 831 patients vs 35 [8%] of 424 patients, p=0·0155). The posterior probability that the bioresorbable polymer sirolimus-eluting stent is non-inferior to the durable polymer everolimus-eluting stent was 100% (Bayesian analysis, difference in target lesion failure frequency −2·6% [95% credible interval −5·5 to 0·1], non-inferiority margin 3·85%, n=2208).

**Interpretation:** The outperformance of the ultrathin, bioresorbable polymer sirolimus-eluting stent over the durable polymer everolimus-eluting stent in a complex patient population undergoing percutaneous coronary intervention suggests a new direction in improving next generation drug-eluting stent technology.


Abstract:

**Objectives:** Spasticity remains highly prevalent in patients with spinal cord injury and multiple sclerosis. To summarize the effects of cannabinoids compared with usual care, placebo for spasticity due to multiple sclerosis (MS) or paraplegia.
Methods: Searches of MEDLINE, EMBASE, CENTRAL and LILACS to March 2017 were performed to identify randomized controlled trials. The primary outcomes were spasticity and spasm frequency. The criteria were any patient with MS and spasticity affecting upper or lower limbs or both, and that had a confirmed diagnosis of MS based on validated criteria, or however defined by the authors of the included studies.

Results: 16 trials including 2597 patients were eligible. Moderate-certainty evidence suggested a non-statistically significant decrease in spasticity (standardized mean difference (SMD) 0.36 [confidence interval (CI) 95% −0.17 to 0.88; p = 0.18; I2 = 88%]), and spasm frequency (SMD 0.04 [CI 95% −0.15 to 0.22]). There was an increase in adverse events such as dizziness (risk ratio (RR) 3.45 [CI 95% 2.71–4.4; p = 0.20; I2 = 23%]), somnolence (RR 2.9 [CI 95% 1.98–4.23; p = 0.77; I2 = 0%]), and nausea (RR 2.25 [CI 95% 1.62–3.13; p = 0.83; I2 = 0%]).

Conclusions: There is moderate certainty evidence regarding the impact of cannabinoids in spasticity (average 0.36 more spasticity; 0.17 fewer to 0.88 more) due to multiple sclerosis or paraplegia, and in adverse events such as dizziness (419 more dizziness/1000 over 19 weeks), somnolence (127 more somnolence/1000 over 19 weeks), and nausea (125 more somnolence/1000 over 19 weeks).


Abstract:

Background: Oral anticoagulation is underused in patients with atrial fibrillation. We assessed the impact of a multifaceted educational intervention, versus usual care, on oral anticoagulant use in patients with atrial fibrillation.

Methods: This study was a two-arm, prospective, international, cluster-randomised, controlled trial. Patients were included who had atrial fibrillation and an indication for oral anticoagulation. Clusters were randomised (1:1) to receive a quality improvement educational intervention (intervention group) or usual care (control group). Randomisation was carried out centrally, using the eClinicalOS electronic data capture system. The intervention involved education of providers and patients, with regular monitoring and feedback. The primary outcome was the change in the proportion of patients treated with oral anticoagulants from baseline assessment to evaluation at 1 year. The trial is registered at ClinicalTrials.gov, number NCT02082548.

Findings: 2281 patients from five countries (Argentina, n=343; Brazil, n=360; China, n=586; India, n=493; and Romania, n=499) were enrolled from 48 clusters between June 11, 2014, and Nov 13, 2016. Follow-up was at a median of 12·0 months (IQR 11·8–12·2). Oral anticoagulant use increased in the intervention group from 68% (804 of 1184 patients) at baseline to 80% (943 of 1184 patients) at 1 year (difference 12%), whereas in the control group it increased from 64% (703 of 1092 patients) at baseline to 67% (732 of 1092 patients) at 1 year (difference 3%). Absolute difference in the change between groups was 9·1% (95% CI 3·8–14·4); odds ratio of change in the use of oral anticoagulation between groups was 3·28 (95% CI 1·67–6·44; adjusted p value=0·0002). Kaplan-Meier estimates showed a reduction in the secondary outcome of stroke in the intervention versus control groups (HR 0·48, 95% CI 0·23–0·99; log-rank p value=0·0434).

Interpretation: A multifaceted and multilevel educational intervention, aimed to improve use of oral anticoagulation in patients with atrial fibrillation and at risk for stroke, resulted in a significant increase in the proportion of patients treated with oral
anticoagulants. Such an intervention has the potential to improve stroke prevention around the world for patients with atrial fibrillation.

**Funding:** Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, and Pfizer.


**Abstract:**

**Objectives:** GuiZhi-ShaoYao-ZhiMu decoction (GSZD), a traditional Chinese herbal medication for the management of rheumatoid arthritis (RA), has a long history of use and modern scientific research support for efficacy, but the studies have not been systematically evaluated. Therefore, this study systematically reviewed the efficacy of GSZD using the available human clinical trials and conducted a meta-analysis.

**Methods:** The available databases were searched using proper languages of English, Korean, and Chinese. The key terms used for searching were “GSZD,” “Cassia Twig,” “Guizhi,” “Paeonia lactiflora,” “Shaoyao,” “Anemarrhena Rhizome,” “Zhimu,” “rheumatoid arthritis,” “randomized,” “controlled trial,” and “clinical trial.” Randomized clinical trials (RCTs) using GSZD were included in the review and meta-analysis. According to heterogeneity, odds ratio and confidence intervals in the pooled RCTs were assessed by a fixed or random model in meta-analysis. Risk of bias was evaluated for all included studies.

**Results:** Thirteen RCTs met the inclusion criteria and were included in the meta-analysis. All studies evaluated the efficacy of GSZD for treating RA, but the herbal formulations varied since some studies added herbs to the basic GSZD formulation. However, all formulations contained the essential herbs: Guizhi, Shaoyao, and Zhimu. Each RCT included an experimental group (GSZD with or without Western-style medicine) and a control group (either standard Western-style medicines or placebo). When compared to placebo, the GSZD treatment was found to be three to six times more effective than standard Western drugs for some symptoms. Furthermore, only two studies reported any adverse events associated with the GSZD group, whereas several reported serious adverse events in the control groups.

**Conclusions:** The Traditional Chinese Medicine, GSZD, may have equal or superior effectiveness and safety for treating RA compared to Western RA drugs. It should be considered a viable alternative to Western medicine. However, more long-term research is needed in larger patient groups to better establish its safety and efficacy.

