e-CHLAS

November 2018

CCRH LIBRARY
PREFACE

Introduction

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

Scope

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

Arrangement of Entries

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

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

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(Meenakshi Bhatia)
Librarian
AYUSH & Other Systems


Abstract:

Introduction: This study was performed to evaluate the clinical effect of a Korean medicine treatment for livedoid vasculopathy (LV).

Methods: Five patients with LV were selected who exhibited blood stasis due to qi stagnation () caused by external cold () or dual deficiency of qi and blood () and who had suffered from chronic episodic LV for at least 2 years. The treatment consisted of Korean herbal medicine, Haechungtang (HC). Five cases were evaluated based on visual symptoms. The symptoms at first visit were scored on a visual analogue scale (VAS) from 1 to 10.

Results: Following treatment, all of the symptoms except pigmentation disappeared completely in all cases. No symptom control with corticosteroids or warfarin was necessary.

Conclusion: These case reports suggest that HC could be effective for treating LV. Follow-up studies and further clinical studies are needed to evaluate recurrence and to provide more efficient treatment.


Abstract:

Objective: The main purpose of this article is to report the systematic data collection pertaining to the consultations of a group of qualified homeopathic physicians. Studies have been performed concerning: (1) the most frequently treated pathologies; (2) the symptoms reported by patients, with a particular focus on “fear” symptoms; and (3) the evaluation of the outcomes of the treatment, including likelihood ratio (LR) for fear symptoms of mostly prescribed remedies.

Design: Prospective observational study.

Setting: Individualized homeopathic treatment at private homeopathic surgeries in Italy.

Participants: Adult patients asking for homeopathic therapy for a series of common ailments.

Outcome Measures: Types of diseases and remedies used and clinical parameters (frequency of acute attacks, and their intensity and duration); the
overall outcome of the cure was registered using the Outcome Related to Impact on Daily Living (ORIDL) scale.

**Results:** Only 94 patients could be enrolled by eight homeopathic doctors in a 2-year period between 2015 and 2017. Ninety (72 females, 18 males) patients completed the observation period. The most represented pathologies belonged to the group “Anxiety and anxiety disorders” followed by gastrointestinal ailments. The most prescribed remedy was Phosphorus (9 cases), followed by Natrum muriaticum (4 cases) and Ignatia (4 cases). The intensity of the symptoms and the frequency of the attacks decreased during the course of the study. Most patients reported a positive outcome (ORIDL scale). In the “Phosphorus” group, LR values were calculated for fear symptoms: LR for fear of dark $\frac{1}{4}$ 2.25 (95% confidence interval [CI] $\frac{1}{4}$ 0.56 to 9.02), LR for fear of crowds $\frac{1}{4}$ 1.27 (95% CI $\frac{1}{4}$ 1.13 to 1.42), and LR for fear of ghosts $\frac{1}{4}$ 1.12 (95% CI $\frac{1}{4}$ 1.04 to 1.22).

**Conclusion:** The recruited group was smaller than expected, but data from most participants could be collected. Positive clinical outcomes were recorded and LR of a few specific fears contributed to distinguish Phosphorus patients from the remaining population.

**Atis Filiz Yarici, Rathfisch Gulay. Effect of hypnobirthing training given in the antenatal period on birth pain and fear. Complementary Therapies in Clinical Practice 2018; (33): 77-84p.**


**Abstract:**

**Background** During chemotherapy, the correlation between insomnia and fatigue, anxiety, pain, depressed mood, and cognitive disorders makes these subjective complaints a ‘symptom cluster’ with common biological mechanisms. The theory of cerebral inflammation following the production of pro-inflammatory cytokines (high level of interleukin 1-β [IL1-β], IL6 and tumour necrosis factor-alpha) is currently the most generally accepted. Understanding these mechanisms should allow us to propose a chemoprotective homeopathic treatment of the nervous system.

**Methods** By retaining the inflammatory aetiology, we combined the rubrics ‘Inflammation of the brain’, ‘Inflammation of the meninges’, ‘Inflammation of the nerves’ with the symptom cluster: insomnia, fatigue, depressive state and memory disorders.

**Results** After repertorisation, we propose the following homeopathic protocol: *Belladonna* 15c, *Phosphorus* 15c, Cerebral cortex 4c and Nerves 4c, two pills of each medicine to be sucked together before breakfast, lunch and dinner, on each day of chemotherapy and for the following 2 days.
Conclusion  This selected protocol, derived from a physiopathological knowledge of the symptoms, seems to be well suited to the prevention and treatment of post-chemotherapeutic cerebral inflammation. It is essential to start the homeopathic treatment before the chemotherapy session to anticipate the emergence of the ‘chemo-brain’ side effects. This proposed prevention protocol must be confirmed and quantified by randomised studies.


Abstract:

Background and Purpose: Existing research suggests that both massage and essential oils may have analgesic and anti-inflammatory benefits. We investigate the benefits of the Aroma Touch Hand Technique® (ATHT), a procedure that combines a moderate pressure touch with the application of essential oils to the hand, in individuals with hand arthritis.

Methods and materials: Thirty-six participants with rheumatoid arthritis, osteoarthritis, and/or chronic inflammation received ATHTs with either a 50/50 preparation of Deep Blue® and Copaiba oil or a coconut oil placebo twice daily for 5 consecutive days. Changes in maximum flexion in finger and thumb joints, items from the Arthritis Hand Function Test, and hand pain scores were evaluated.

Results: Participants treated with the essential oil preparation required significantly less time to complete dexterity tasks and showed about 50% decrease in pain scores, increased finger strength, and significantly increased angle of maximum flexion compared to subjects treated with coconut oil.

Conclusion: The ATHT with Copaiba and Deep Blue may have ameliorative effects on hand arthritis.


Abstract:

Background and purpose: We evaluated the feasibility of using an activity monitor to support mindfulness practice, reduce self-reported stress and physiological indicators of stress.
**Materials and methods:** Adult women (N = 19) who previously participated in a mindfulness intervention wore an activity monitor for eight-weeks. The activity monitor notified them when they were stressed (based on standard deviation pulse pressure). Heart rate and pulse pressure were continuously collected via the activity monitor. Mindfulness, stress, depression and trauma symptoms were collected via self-report surveys.

**Results:** There were no significant changes in self-reported stress, depression, post-traumatic stress and mindfulness from baseline to eight-weeks. Pulse pressure and standard deviation of pulse pressure increased over time. Those who were high on the non-judge mindfulness subscale had a lower standard deviation pulse pressure and spent less time stressed.

**Conclusion:** Those who are more mindful are less likely to have physiological signs of stress.


**Abstract:**

Individuals with Parkinson's disease (PD) typically display symptoms of rigidity, bradykinesia, and postural instability that can limit participation in recreational activities. The purpose of this clinical report is to describe the development, implementation, and outcomes of a novel and innovative community-based golf and exercise program for individuals with PD. In response to community interest, the program was developed through a unique partnership that blended the expertise of physical therapists and golf professionals. The 6-week program consisted of golf instruction and task-specific exercises. Improvements were noted in seven of eight participants for golf performance (driving distance and club head speed) and quality of life (PD Questionnaire-39) outcome measures. This report describes the design and implementation of a golf and exercise program for people with PD based on community need, evidence, and clinical expertise. Considerations and recommendations for future programs are discussed, such as program length, staffing, volunteers, funding, location, and resources.

**Chunawala Aafreen, Jain Pratik. Breath of Fresh Air. Homoeopathic Links 2018; 31(3): 198-203p.**

**Dane Senol, Welcome Menizibeya O. Case study: Effects of foot reflexotherapy on ADHD symptoms and enuresis nocturia in a child with ADHD and enuresis nocturia. Complementary Therapies in Clinical Practice 2018; (33): 139-41p.**
Abstract:

**Background and purpose:** Symptoms of Attention-Deficit Hyperactivity Disorder (ADHD) can occur in association with enuresis nocturia. Alternative therapies may be effective in addressing the maladies of children with ADHD comorbidities. The purpose of this study was to investigate the effects of foot reflexotherapy in a child with ADHD and enuresis nocturia.

**Materials and methods:** The patient was an 8-year-old child with ADHD and enuresis nocturia. Pre- and post-tests for ADHD were completed using Vanderbilt ADHD Diagnostic Teacher Rating Scale. The subject was treated with foot reflexotherapy for 20-min per session twice per week for a period of 8 weeks.

**Results:** The child showed improvement in ADHD symptoms and his enuresis nocturia disappeared completely after foot reflexotherapy.

**Conclusion:** Foot reflexotherapy was effective in improving inattention, hyperactivity in the child with ADHD. The results of this novel study suggest that foot reflexotherapy can be effective in treating ADHD child with enuresis nocturia.


Abstract:

**Background:** Cough preparations containing aqueous marshmallow root extracts (Althaea officinalis) have a long history as medicinal products in Germany. The aim of the 2 prospective, non-interventional surveys reported here was to create a better documentation of the users' impression of the effectiveness and tolerability, and user satisfaction.

**Methods:** Consumers (n = 822) buying either lozenges or syrup of the aqueous marshmallow root extract STW42 to treat their dry cough were recruited in pharmacies in 2 independently performed surveys. They were asked to fill in a questionnaire covering a treatment duration of 7 days so that the course of symptoms could be documented, and the overall effectiveness, tolerability and satisfaction assessed.

**Results:** This consumer-reported outcome shows that both preparations showed a good effect with respect to the symptomatic treatment of oral or pharyngeal irritation and associated dry cough with a very rapid onset of effects, in the majority of cases within 10 min. The tolerability was very good (with only 3 minor adverse events for the syrup).
Conclusion: The results of the surveys justify the long-established use of both marshmallow preparations for symptomatic treatment of dry cough.


Abstract:

**Background and purpose:** Mental practice of motor imagery has shown beneficial effects in stroke recovery. However, there are few clinical trials investigating it on the subacute phase. This study will investigate the effects of mental practice in the mobility of patients with subacute stroke.

**Materials and methods:** Randomized controlled trial including persons with subacute stroke (<3 months). All participants will receive physical exercises and will be randomly allocated into an experimental group (Mental Practice) or into a control group (cognitive training) for 4 weeks (12 sessions).

**Results:** Primary outcomes will be assessed at baseline and after intervention and will be related to mobility, using Timed Up and Go test and 5 m walking speed test. Whereas secondary outcomes will be muscular strength, biomechanical strategies, mental health and quality of life.

**Conclusion:** The beneficial effects that may be found in this trial can be greatly relevant in clinical practice, justifying this scientific question.


Abstract:

**Background:** Benign prostatic hyperplasia (BPH) is one of the most common diseases in age group above 50 years. Symptoms relating to urination are usually frequency, urgency, and hesitancy and vary from case to case. Very few studies are reported on homoeopathic treatment of BPH. Hence, an evidence-based observational study on five patients of BPH was done using homoeopathic medicines. The objective of this case series is to assess the usefulness of individualised homoeopathic medicines in the treatment of cases of BPH.

**Methodology:** An open-label observational prospective study was done on patients of BPH at Gaurang Clinic and Centre for Homoeopathic Research, Lucknow, Uttar Pradesh, India, and five patients included in this cases series were treated during 2007–2009. Individualised homoeopathic medicines were prescribed to these patients, after proper case taking, repertorisation and consultation of Materia Medica. Patients were assessed using parameters like
International Prostate Symptom Score, uroflowmetry, ultrasonography and prostate-specific antigen.

**Results:** Baseline and post-treatment parameters were assessed, which showed significant improvement in post-treatment values along with relief of symptoms in all five patients.

**Conclusion:** Results of the study are encouraging and in accordance with the basic principles of homoeopathic prescribing (i.e. classical approach), exhibiting the benefits of constitutional medicines. All the patients showed improvement in their symptoms and laboratory parameters. However, studies with larger sample size and randomised controlled trial study design are suggested.


**Abstract:**

**Background and purpose:** In the East-Asian countries, the combined treatment of Western medicine and herbal medicine has been widely administered. The purpose of this study was to evaluate the efficacy and safety of herbal medicine in the treatment of acute ischemic stroke.

**Methods:** We searched the PubMed, Cochrane Central Register of Controlled Trials, EMBASE, and CNKI up to January 2017. Randomized Controlled Trials evaluating the effect of adjunctive herbal medicine on acute ischemic stroke were included.

**Results:** A total of 80 studies (8057 patients) were collected. The overall methodological quality was low. In the herbal group, meta-analysis indicated a statistically significant improvement in the neurologic deficits and activity of daily living compared with the non-herbal group. Furthermore, herbal treatments were relatively safe.

**Conclusion:** The treatment can induce neurological improvements without side effects. However, concrete conclusions cannot be made due to the methodological problems of the included studies.


**Abstract:**

**Background and objective:** According to basic studies, hot spring use has positive effects on the mind and body. However, the association between habitual hot spring use and prevention of long-term care is unknown. Using
long-term care insurance data for the residents of Atami City, Japan, who can choose to install hot spring water supply in their homes, this study aimed to determine the association between the installation of a hot spring water supply in the home and prevention of long-term care.

**Methods:** 1. Study design: case-control study 2. Subjects: 2719 residents (754 men, 1965 women) of Atami City, Shizuoka Prefecture, Japan, who received long-term care insurance and were certified as “Needing Support” or “Needing Long-Term Care” as of March 2017. 3. Survey methods: Information on long-term care insurance certification was linked to subjects’ care level dating back to their initial certification. Also, the installation (or lack thereof) of hot spring water supply in each subject’s home was linked to information on Atami household water use as of March 2017. 4. Analysis methods: The age distribution of the subjects was determined. Initial care status and care status as of March 2017 were then compared for the 2194 subjects who received long-term care certification at least twice. These subjects were classified into two groups: those whose care level had not changed or had improved (no change/improvement group) and those whose care level had worsened (worsening group). Subjects were then compared by sex and initial care level in terms of hot spring installation and percentages of no change/improvement or worsening of care level; odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using the chi-square test. Lastly, the same analysis was performed for all subjects grouped together, and ORs and 95% CIs were calculated using the Mantel-Haenszel test.

**Results:** Hot springs were installed in the homes of 2359 subjects overall (86.8%). The no change/improvement group and the worsening group comprised 1192 and 1002 subjects, respectively. Overall, improvement or no change in care level was observed in 1050 subjects (55.2%) in the hot spring group and 142 subjects in the no hot spring group (48.5%). Sex-adjusted OR (95% CI) was 1.311 (1.025–1.677, \( p = 0.036 \)), which represented a significant association. Having a hot spring water supply in the home may be associated with preventing worsening of care level.

**Conclusion:** Having a hot spring water supply in the home may be associated with preventing worsening of care level.


**Abstract:**

**Background and purpose:** This study investigated the disclosure of complementary and alternative medicine (CAM) use to health care providers by Malaysian thalassemia patients.

**Methods:** The semi-structured interviews were audio taped, transcribed verbatim, and translated into English.
Results: Thematic analysis identified four themes: 1) reason for CAM disclosure, 2) attempt to disclose CAM, 3) withdrawal from CAM disclosure, and 4) non-disclosure of CAM use. The reason for patients' disclosure of CAM use to healthcare providers is because they wanted to find information about CAM and were afraid of the interaction between the conventional medicine and CAM. Patients also disclosed the use of CAM because they were not satisfied with the conventional medicine that had caused them harm.

Conclusion: Effective communication between patients and health care providers is important, especially for patients who are undergoing conventional thalassemia treatment, for fear that there is an interaction between conventional treatment and CAM use.


Abstract:

Background: Primary dysmenorrhea is a cyclic cramp in pelvic which interferes with daily activity. This study determined the effect of Cinnamon on relieving dysmenorrhea.

Methods: This is a randomized, double-blind clinical trial. The intervention group received Cinnamon (capsules contained 1000 mg cinnamon) and the control group received placebo (capsules contained 1000 mg starch) during the first 72 h of menstruation for two cycles continuously. The Visual Analogue Scale was used to determine the severity of pain. The subjects were followed up for two cycles. Descriptive statistics, Independent T test, analysis of variance (ANOVA) with repeated measures were used for continuous quantitative variables. Mann-Whitney and Chi-square tests were used for nominal and ordinal qualitative variables.

Results: The results showed the mean intensity of dysmenorrhea significantly decreased over time in both groups (time: P < 0.001) and this reduction was significantly different over time between two groups (time*group: P = 0.02). There is significantly more reduction in the intervention group. Also the pain reduction in the intervention group was significantly lower than the placebo group after the first treatment (P = 0.001) and the second treatment (P = 0.002) compared to before treatment.

Conclusions: Cinnamon can reduce the intensity of primary dysmenorrhea. This aromatic spice for relieve of primary dysmenorrhea is recommended.


Abstract:

The survival rate of patients with hepatocellular carcinoma and extrahepatic metastases is very poor. Sorafenib, a targeted chemotherapy agent, has been
shown effective for patients with advanced hepatocellular carcinoma (HCC), but it is associated with serious side effects. In addition, although surgery has been regarded as effective for lung metastases from HCC, its use in these patients is limited. Complementary and alternative medicine, including traditional Korean medicine (TKM), is increasingly used in cancer treatment, as it has been found to improve patient quality of life and maintain tumor size. This report describes a 62-year-old Korean woman with lung metastases from HCC. She first underwent surgery (stage IV) and six cycles of adjuvant chemotherapy. She was subsequently treated with sorafenib, but computed tomography showed progressive disease and she experienced the side effects of sorafenib. The patient started treatment with TKM, including pharmacopuncture and herbal medicine, in addition to sorafenib. After 8 weeks of TKM treatment, the size of the metastatic nodules decreased and the sorafenib-associated side effect symptoms improved. These findings suggest that treatment with a combination of TKM and sorafenib may be a promising method for patients with HCC and extrahepatic metastases.


Abstract:

Background and purpose: Medical cannabis may be effective treatment for refractory epilepsy. It is timely to seek users' and potential users' opinions in regard to its place in the management of epilepsy.

Materials and methods: An online survey was administered to members of an epilepsy support organisation in Western Australia. Experience with cannabis for management of epilepsy was explored, along with desire to trial a particular pharmaceutical formulation(s).

Results: People with epilepsy (33/71) and carers (38/71) participated. Fifty-four participants indicated no experience with medical cannabis, although 35, mainly with inadequate response to prescription medicines, were willing to ask for a prescription. Concerns included difficulty accessing cannabis and high cost of this treatment. Tablets/capsules was the most acceptable dosage form for development.

Conclusion: These findings suggest wide interest in trialling medical cannabis in individual cases of refractory epilepsy, despite the developing body of literature and some concerns about cost and procurement.

Kienle Gunver S, Mussler Milena, Fuchs Dieter et al. Subjective dimension of integrative cancer care: A qualitative study exploring the perspectives, themes, and observations of experienced doctors from the area of
Abstract:

**Background:** Integrative cancer care (ICC) is used by approximately 50% of cancer patients to complement oncologic treatments and to address unmet needs. One ICC practice is anthroposophic medicine, integrating conventional and complementary cancer care. It specifically provides mistletoe therapy (MT), but also intensive counselling, natural remedies, creative and movement therapies, nursing procedures, nutrition, and others. The objective of this study was to explore perceptions, themes, goals, procedures, and observations of experienced AM doctors with regard to the subjective dimensions of ICC.

**Method:** A guideline-based qualitative interview study was conducted with 35 AM doctors working in hospitals and office-based practices in Germany and other countries. Structured qualitative content analysis was applied to examine the data. Triangulation was done with published studies investigating patients’ perspectives on AM and MT.

**Results:** The interviewed doctors integrated conventional and holistic cancer concepts. Overarching therapeutic themes were: to enable patients to live with or overcome their disease, to find their own way through their disease, and to possibly reframe their situation. A broad variety of therapeutic goals were pursued, depending on the situation and priorities of the particular patient. Doctors described varying levels of patients’ improved strength; increased vitality, thermal comfort, and recovery; relief from suffering, particularly in the areas of fatigue, appetite, sleep, pain, infections, and reactions to toxic anti-cancer therapies. The doctors also described how they perceived changes of patients’ emotional level, their coping, autonomy, functional abilities, and finding their own way to deal with the disease. This is consistent with patients’ perspectives described in published studies.

**Conclusion:** Themes, goals, and described benefit of ICC from doctors’ and patients’ perspective may be an important complementation of conventional cancer care, as it meets important needs, distresses and conditions of patients which often stay unmet and unrelieved. Further research should investigate these goals and procedures.


Abstract:
Introduction: In overseas reports, temporomandibular disorders (TMDs) are said to affect 5–12% of the population, and the number of TMD patients seeking treatment in Korea is on the rise. Even though Korean medicine (KM) treatments are commonly used for TMDs in clinical practice, clinical practice guidelines (CPGs) for TMDs in traditional KM have not yet been established. This evidence-based KM CPG on TMDs was therefore established.

Methods: The key questions of the KM CPG on TMDs were determined based on clinical practice surveys on the use of KM for TMDs and expert opinion from the relevant academic societies by the CPG development committee. Then, a systematic literature review of KM treatments for TMDs was conducted for each key question, and the guideline draft was created in accordance with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) levels of evidence and grades of recommendation. Official consensus was achieved using the Delphi method on the draft, and the draft was further revised through external review to produce the final guideline, which was certified by the relevant academic societies.

Results: A total of 15 recommendations are established to address the 13 key clinical questions about the clinical efficacy of 9 types of KM treatments for TMD, including grades and levels of evidence.

Conclusions: The present guideline is expected to aid in the decision-making process of physicians and TMD patients, improve the overall quality of KM practice, and suggest subjects for future clinical research.


Abstract:

Background: Hemarthrosis is a common clinical presentation of patients with severe and moderately severe hemophilia. Severe pain, swelling, and loss of function involving knee, ankle, elbow, and shoulder joints are commonly seen. In India, except for paracetamol and some non-steroidal anti-inflammatory drugs (NSAIDs), opiate analgesics are not easily available even in the mainstay of treatment; i.e., factor concentrates are also not available regularly. Hence, there is an unmet need for exploring alternative management strategies in this condition in India.

Objective: To assess the effect of homeopathic medicines on pain and acute hemarthrosis in hemophilia when factor concentrates are not available and paracetamol in adequate doses proves inadequate.

Patients: 343 patients with hemophilia (PWH) from Nashik, Mumbai, and Surat presenting with hemarthrosis were prescribed homeopathic medicines in addition to paracetamol and RICE (rest, immobilization, cold application, and elevation). They were assessed using standard techniques.
Results: 1,679 episodes of hemarthrosis in major joints were encountered between December 2007 and March 2014, in 343 patients. In 1,580 of the 1,679 hemarthrosis episodes (94.1%), bleeding/inflammation was arrested and pain relieved with homeopathic medication. Additional factor concentrate was required in 99 patients (4.48%). The mean pain score improved from 6.88 ± 2.118 to 1.5 ± 0.34 over 6-24 h following the homeopathic medicines (p < 0.0001). The swellings were also substantially reduced (p < 0.001). The number of joint bleeds per month was reduced significantly under the influence of therapy (p < 0.0001), showing the long-term disease-modifying effect of the treatment.

Conclusion: Homeopathic medicines without factor concentrates appeared to reduce bleeding and pain in PWH presenting with hemarthrosis and could have influenced the long-term frequency of bleeding.


Abstract:

The World Health Organization strategy for global health includes a culturally-sensitive blending of western biomedicine with traditional forms of healing; in practical terms this approach is often referred to as integrative medicine. One distinct element within the systems of North American integrative healthcare is naturopathic medicine; while the basic premise of its fundamental approach to care – supporting healthy lifestyle behaviors – is as old as medicine itself, the early history of organized naturopathy in North America was heavy in theory and light on critical analysis. Dozens of questionable modalities and protocols have been housed under the rubric of naturopathy. It is our contention that the progression of professional naturopathic medicine in the 21st century – with goals of personal, public and planetary health – requires the active pursuit of critical analysis. We examine the primary guiding principles which drive the training and practice of North American naturopathic medicine; while these principles are laudable in the age of patient-centered care, we argue that there are shortcomings by absenteeism. We propose a seventh principle – Scientia Critica; that is, the ability to critically analyze accumulated knowledge – including scientific facts, knowledge about the self (critical consciousness) and values of the patient.

Abstract:

Introduction: Many Chinese traditional medicines provide good therapeutic effects. To screen their pharmacological activities and to discover new bioactive constituents, a SYBR® Green real-time PCR method was established based on information of the melanogenesis-related genes sequences.

Methods: Specific primers were designed according to the sequences of melanogenesis-related genes TYR, TRP-1, TRP-2 and MITF, to establish and optimize a quantitative real-time PCR reaction system based on treatment with 8-methoxypsoralen. Using this system, the effects of Vernonia anthelmintica (L.) Willd injections, Muniziqi granules, Suziafu tablet, Atirilali tablet, Yiti 'erfeili Aikemuaili Migao and Bairesi Migao on the expression of TYR, TRP-1, TRP-2 and MITF in mouse melanoma B16 cells were assessed.

Results: Primers were designed to be specific to melanogenesis-related genes, and standard curve was constructed using recombinant plasmids containing gene fragments. Cycle thresholds and the template concentrations showed a good linear relationship, the absorption peak of the dissociation curves was single, correlation coefficients were between 0.983 and 0.999, and amplification efficiencies was between 100.95% and 103.05%. A significant positive correlation was observed between the drug concentration (from 25 to 100 μM) and gene expression after 24 h treatment, although Muniziqi granules and Yiti 'erfeili Aikemuaili Migao had not passed this route.

Conclusion: Real-time PCR was shown to verify compounds with bioactivities that promote melanin production. It also validated that 8-methoxypsoralen and some traditional medicines increased melanin production by increasing the expression of TYR, TRP-1 and TRP-2 and MITF in B16 cells.


Abstract:

Introduction: Meditation has attracted increased attention in the literature as a non-pharmacological strategy to foster positive mental health amongst the general population. This systematic review aims to summarise studies of mantra meditation (which includes Transcendental Meditation, TM®) to understand its potential value in fostering positive mental health and alleviating negative affectivity in non-clinical populations.

Methods: Electronic databases were searched for English language, peer-reviewed empirical studies (published between 1970 and 2018) that related to mantra meditation, reported at least one outcome of mental health and utilised healthy, non-clinical populations. Studies were assessed for quality and risk of bias using the Quality Appraisal Tool for Quantitative Studies (QATQS). Data abstraction was facilitated by a tailored data extraction form.
Results: A total of 2171 records were identified, of which 37 were included in this review. Studies report on outcomes of anxiety, stress, depression, burnout, anger and psychological distress. 78% of studies utilised the TM programme. Findings indicate that mantra meditation interventions may have minimal to moderate beneficial effects on mental health in general populations. Over 90% of studies were considered to be of weak quality.

Conclusions: There is some evidence that mantra meditation can improve mental health and negative affectivity in non-clinical populations, however poor study quality may hinder the extent to which one can be certain about the accuracy of these findings. Mantra meditation may be considered a useful adjunct to workplace wellbeing initiatives or educational programmes. Further studies of higher quality that incorporate cost-effectiveness analyses are warranted.


Abstract:

Background: This study focuses on randomised controlled trials (RCTs) of individualised homeopathic treatment (IHT) in which the control (comparator) group was other than placebo (OTP).

Aims: To determine the comparative effectiveness of IHT on health-related outcomes in adults and children for any clinical condition that has been the subject of at least one OTP-controlled trial. For each study, to assess the risk of bias and to determine whether its study attitude was predominantly ‘pragmatic’ or ‘explanatory’.

Methods: Systematic review. For each eligible trial, published in the peer-reviewed literature up to the end of 2015, we assessed its risk of bias (internal validity) using the seven-domain Cochrane tool, and its relative pragmatic or explanatory attitude (external validity) using the 10-domain PRECIS tool. We grouped RCTs by whether they examined IHT as an alternative treatment (study design Ia), adjunctively with another intervention (design Ib), or compared with a no-intervention group (design II). For each RCT, we identified a ‘main outcome measure’ to use in meta-analysis: ‘relative effect size’ was reported as odds ratio (OR; values >1 favouring homeopathy) or standardised mean difference (SMD; values < 0 favouring homeopathy).

Results: Eleven RCTs, representing 11 different medical conditions, were eligible for study. Five of the RCTs (four of which in design Ib) were judged to have pragmatic study attitude, two were explanatory, and four were equally pragmatic and explanatory. Ten trials were rated ‘high risk of bias’ overall: one of these, a pragmatic study with design Ib, had high risk of bias solely regarding participant blinding (a bias that is intrinsic to such trials); the other trial was rated ‘uncertain risk of bias’ overall. Eight trials had data that were
extractable for analysis: for four heterogeneous trials with design Ia, the pooled OR was statistically non-significant; collectively for three clinically heterogeneous trials with design Ib, there was a statistically significant SMD favouring adjunctive IHT; in the remaining trial of design 1a, IHT was non-inferior to fluoxetine in the treatment of depression.

**Conclusions:** Due to the low quality, the small number and the heterogeneity of studies, the current data preclude a decisive conclusion about the comparative effectiveness of IHT. Generalisability of findings is limited by the variable external validity identified overall; the most pragmatic study attitude was associated with RCTs of adjunctive IHT. Future OTP-controlled trials in homeopathy should aim, as far as possible, to promote both internal validity and external validity.


**Mengelberg A, Leathem J, Podd J. Fish oil supplement use in New Zealand: A cross-sectional survey.** *Complementary Therapies in Clinical Practice 2018; (33): 118-23p.*

**Abstract:**

**Objective:** The aims of the survey were to determine: (i) the percentage of fish oil supplement users in a sample population; (ii) why people take fish oil supplements; (iii) where fish oil supplements are stored as well as the average daily dosage; (iv) what dietary and lifestyle behaviours are associated with fish oil supplement use.

**Design:** An online cross-sectional survey.

**Setting:** New Zealand.

**Respondents:** A total of 334 New Zealand residents over the age of 18.

**Results:** Fish oil supplements were taken by 21.9% of respondents. Reasons for taking fish oil supplements were - 72.6% for ‘general well-being’, 54.8% to ‘improve brain function’, 31.5% for ‘pain/inflammation’, 12.3% to ‘lower cholesterol levels’ and 11% for ‘a dietary insufficiency’. Approximately 26% of fish oil users reported taking a dose of fish oil supplements that would meet the recommended daily intake of 400–600 mg combined docosahexaenoic acid and eicosapentaenoic acid, and only 6.8% of fish oil users reported storing their fish oil supplements in the refrigerator. After controlling for other characteristics including age, gender, ethnicity and body mass index, fish oil supplementation use was most likely among respondents who already eat oily fish and least likely in respondents who regularly eat nuts and seeds.

**Conclusions:** Fish oil supplements are a commonly used supplement in New Zealand, yet questions remain about the role of these supplements in improving health outcomes. Safety issues related to manufacturing and
storage conditions indicate that there is an urgency in answering these questions.


**Abstract:**

**Background:** Neck pain is one of the commonest complaints and an important public health problem across the globe. Yoga has reported to be useful for neck pain and hot sand has reported to be useful for chronic rheumatism. The present study was conducted to evaluate the add-on effect of hot sand fomentation (HSF) to yoga on pain, disability, quality of sleep (QOS) and quality of life (QOL) of the patients with non-specific neck pain.

**Material & Methods:** A total of 60 subjects with non-specific or common neck pain were recruited and randomly divided into either study group or control group. Both the groups have received yoga and sesame seed oil (*Sesamum Indicum L.* ) application. In addition to yoga and sesame seed oil, study group received HSF for 15 min per day for 5-days. Assessments were taken prior to and after the intervention.

**Results:** Results of the study showed a significant reduction in the scores of visual analogue scale for pain, neck disability index (NDI), The Pittsburgh Sleep Quality Index (PSQI), and a significant increase in physical function, physical health, emotional problem, pain, and general health both in study and control groups. However, reductions in pain and NDI along with improvement in social functions were better in the study group as compared with control group.

**Conclusion:** Results of this study suggest that addition of HSF to yoga provides a better reduction in pain and disability along with improvement in the social functioning of the patients with non-specific neck pain than yoga alone.


**Abstract:**

**Introduction:** Orbignya speciosa (babaçu) and Mauritia flexuosa (buriti) are palm trees originating in Brazil whose fruits are rich in fixed edible oils that are used for many purposes in the industry. The aim of this study was to describe the chemical composition and investigate the antibacterial activity of
the fixed oil of *O. speciosa* and *M. flexuosa* and to verify their possible effects when combined with aminoglycoside antibiotics.

**Methodology:** The composition of the fixed oils was determined by GC–MS. The antibacterial and synergistic effects of oils and antibiotics, alone and in association, were tested by the microdilution method.

**Results:** The content of fatty acids was estimated through the analysis of fixed oils by GC–MS. The fixed oil of *O. speciosa* contained lauric acid as the most representative fatty acid (54.15%). The fixed oil of *M. flexuosa* contained oleic acid (72.14%) as the major constituent. The fixed oils were examined for antibacterial activity alone and in combination with aminoglycosides. The results show the inhibitory activity of the fixed oils against the bacteria used. The major inhibitory activities were observed for *Escherichia coli* 27 (MIC 32 μg/mL), *Staphylococcus aureus* 358 (MIC 256 μg/mL), and *E. coli* ATCC 25922 (MIC 512 μg/mL) when the fixed oil of *O. speciosa* was used. The synergistic effect was verified with significant values (p < 0.05), which indicates that there is an increase in amikacin activity in the presence of the fixed oil of *O. speciosa*.

**Conclusions:** According to the results obtained, the fixed oil of *O. speciosa* showed significant synergistic effects when combined with the aminoglycoside antibiotic.

**Ooi Soo Liang, McLean Lisa, Pak Sok Cheon. Naturopathy in Australia: Where are we now? where are we heading? Complementary Therapies in Clinical Practice 2018; (33): 27-35p.**

**Abstract:**

Naturopathy is the general practice of natural therapies. It emphasizes prevention, treatment, and promotion of optimal health through therapeutic modalities which encourage the self-healing process of the body. Formalized in the 19th century by the hydrotherapy and nature cure movement in Austria and Germany, naturopathy was introduced to Australia at the turn of the 20th century. It became popular since the 1970s due to social and cultural change characterized by the post-modern philosophy, as well as government policies highlighting individual responsibility and freedom of choice.

Naturopathy is one of the most popular forms of complementary medicine in Australia today with naturopaths received 4.9 million consultations annually. Naturopathic consultations are sought for a variety of conditions and, in some areas, as a form of primary care, especially by middle-aged women who have a higher education level and a higher annual income. The number of Australian naturopaths was estimated to be over 4000 in 2017 and expects to grow to over 4600 by 2022, although this number is likely to be an underestimation.

Australian naturopaths, as a predominantly female profession, work mainly in private clinical practice with nutritional medicine, herbal medicine, homeopathy, as well as massage therapies being the most common modalities used. There are also signs of greater integration with community pharmacies
and integrative medicine clinics in major cities. The Bachelor’s degree programs in Naturopathy has just become the only accredited entry-level qualification since late 2015. Currently, there are only 5 private colleges offering naturopathic education, a far cry from the 40 over in mid-2000.

The profession continues to be self-regulated. There is no barrier of entry to practice and unqualified practitioners of naturopathy can potentially do harm to the public. The registration of naturopaths remains unresolved due to fragmented representation under many professional associations, disunity among the profession, and objections by certain health care lobbyists.

There is a dearth of research demonstrating efficacy of the whole practice of naturopathy in Australia, which has directed the government’s decision to withdraw it from private health insurance coverage from 2019. Moving forward, the whole system research of naturopathy in Australia will be in focus with the recent establishment of a practice-based research network and an international research consortium. With increasing scrutiny from evidence-based medicine, the present and future challenge to Australian naturopaths is centered on the integration of both scientific and traditional evidence to form the foundation of a person-centered, evidence-informed practice.


Abstract:

Aim: To evaluate the short-term effectiveness of connective tissue manipulation (CTM) for relieving menstrual pain and symptoms in primary dysmenorrhea (PD).

Methods: Forty-four women with PD were randomly assigned to treatment (n = 21) or control group (n = 23). While the control group was given only advising, the treatment group additionally received CTM. The primary outcome was the menstrual pain intensity by Visual Analogue Scale. Secondary outcomes included the number of pain medications, menstrual pain catastrophizing by Pain Catastrophizing Scale (PCS), menstrual symptoms by Menstrual Symptom Questionnaire (MSQ) and menstrual attitude by Menstrual Attitude Questionnaire (MAQ).

Results: Compared with the control group, CTM group showed statistically significant improvement in pain, medication use, PCS, MSQ (p = 0.001) and in the perception of menstruation as a natural event (p = 0.029). However, no significant differences were detected between groups for some aspects of MAQ (p > 0.05).

Conclusions: CTM seems to be an effective approach in the short-term in PD.

**Abstract:**

Pride is a secondary emotion that is felt when self-image in the society is at stake. This social emotion is classified into authentic and hubristic pride. Platinum, Palladium, Gratiola, Staphysagria, Sulphur, Lachesis and Veratrum album are few remedies of prime importance mentioned in the homeopathic Materia Medica pertinent to pride. The expression of pride in all the remedies has a particular characteristic feature individualising each remedy. An attempt is made to differentiate the homeopathic medicines attributed to pride in light of modern psychology.


**Abstract:**

**Introduction** The analysis of the periodic table of elements by Jan Scholten opened the way for a new kind of classification and repertorisation of homeopathic remedies. Thereby, group analysis (resorting to series and stages) makes precise prescriptions possible. This approach appears to yield striking results, even in severe cases. Whereas Hahnemann stressed the emotional state (‘Gemüthssymptome’, Organon § 210) when choosing a remedy, Scholten 200 years later investigated the mental picture that represents a life conflict or even a life theme that may maintain the disease process. The person’s environment, emotional traumas or a conflict drives him or her to suppress and dissect painful emotions. Such compensations can become subconscious and so strong that they can no longer be controlled; they then influence the patient with a highly destructive energy.

**Methods** We present five case reports, each dealing with an unusual clinical course of severe cancer associated with homeopathic treatment using the Scholten method.

**Results** By presenting these cases, we consider how the constitution (lifelong signs and symptoms of the patient) and the mental state are interwoven and, as a complex mechanism, might provoke disease.

**Conclusion** The appropriate homeopathic remedy, reflecting the Scholten approach, seemed to have beneficial impact on the disease process of the five individuals presented.


**Abstract:**
**Background and purpose:** Scant information exists about traditional, complementary and alternative medicine (TCAM) use in Indonesia, which prompted investigating its prevalence and correlates in Indonesia.

**Materials and methods:** Participants were 31,415 individuals 15 years and older that participated in the cross-sectional Indonesia Family Life Survey in 2014–15.

**Results:** In all, 24.4% had used a traditional practitioner and/or traditional medicine in the past four weeks, and 32.9% had used complementary medicine in the past four weeks. In adjusted logistic regression analysis, being of older age, being a Muslim, residing in an urban area or on Java, being unhealthy, having a chronic condition, having depression symptoms, experiencing sleep disturbance, and having high social support were associated with both current traditional practitioner and/or medicine use and complementary medicine use.

**Conclusion:** The study shows a high prevalence of TCAM use in Indonesia and several sociodemographic and health related factors of its use were identified.


**Abstract:**

**Objective:** To compare cognition and brain function in elderly Tai Chi and Water Aerobics practitioners.

**Methods:** Eight Tai Chi (TC) and 8 Water Aerobics (WA) practitioners matched by gender, education and age underwent neuropsychological and fMRI scan during attention (Stroop Word Color Task) and working memory (N Back) tasks.

**Results:** Groups were similar for demographic and cognitive variables. Besides anxiety (smaller in TC group), there were no differences between groups in neuropsychological variables. During the Stroop Word Color Task, TC group had smaller brain activation in the right intracalcarine cortex, lateral occipital cortex, and occipital pole, than WA. During N back, TC group presented smaller brain activation in the right frontal pole and superior frontal gyrus.

**Conclusion:** Despite the small number of participants in this preliminary study, both groups had similar cognitive performance, however the Tai Chi group required less brain activation to perform the attention and memory tasks, therefore they may have a more efficient cognitive performance than Water Aerobics group.

*Qi Yan, Zhang Xian, Zhao YiChao et al. Effect of wheelchair Tai Chi on balance control and quality of life among survivors of spinal cord injuries:*

**Abstract:**

**Background:** Wheelchair-related falls are common in survivors with spinal cord injury (SCI). We aimed to assess the effects of wheelchair Tai Chi (WCTC) practice on balance control and quality of life (QOL) among SCI survivors.

**Materials and methods:** Forty SCI survivors were equally divided into WCTC and control groups. The control participants only received the normal rehabilitation intervention, while the WCTC intervention involved 30-min sessions, 2 sessions/day, and 5 days/week for 6 weeks. Static sitting balance, trunk muscle strength, handgrip strength, and QOL were evaluated and statistically analyzed.

**Results:** Compared with the control group, static sitting balance, left handgrip strength, and the psychological domain of QOL improved significantly in the WCTC group (time by group interaction, $p < 0.05$).

**Conclusion:** Six weeks’ WCTC training improved static sitting balance and QOL in survivors with SCI. It may be a feasible, safe, and effective exercise for SCI survivors.


**Abstract:**

Warts are caused by human papilloma viruses (HPV) that can affect any part of the body including hands and feet. Verruca palmaris (VP) is a common manifestation due to HPV infection in keratinocytes of the palms. In the conventional system of medicine, VP is commonly managed through cauterisation, cryosurgery, surgical removal or topical ointments, which have many limitations. Scientific documentation for the treatment of VP by homoeopathic medicines is very scanty. In this context, the present case report is of a 40-year-old male patient, who had multiple warts on his right palm for more than 2 years. The patient was treated previously with allopathic medications and external applications, without any significant improvement. Homoeopathic remedy (i.e. Natrum mur) was initially administered in 30C potency for 30 days, but no improvement was observed in the patient. Interestingly, when the potency was increased to 200C, a speedy recovery was observed and the patient was fully cured within 3 months. Therefore, it can be concluded from the case study that VP, when treated on the basis of the totality of symptoms, with an accurately selected remedy in suitable potency results in cure. In this particular case, Natrum mur worked well for warts on the palm. Most importantly, it was observed in this case that the selection of right
potency is very essential and it should match correctly with the susceptibility of the patient to result in rapid cure.


**Abstract:**

**Background and objective:** The practice of yoga is associated with enhanced psychological wellbeing. The current study assessed the correlation between the duration of yoga practice with state mindfulness, mind-wandering and state anxiety. Also, we examined if an additional 20 min of yoga breathing with intermittent breath holding (experimental group) for 8 weeks would affect these psychological variables more than regular yoga practice (control group) alone.

**Methods:** One hundred sixteen subjects were randomly assigned to experimental ($n = 60$) and control ($n = 56$) groups. State mindfulness attention awareness scale (SMAAS), Mind-Wandering Questionnaire (MWQ) and State anxiety inventory were administered at baseline and at the end of 8 weeks.

**Results:** Baseline assessment revealed a positive correlation between duration of yoga practice with SMAAS scores and negative correlation with MWQ and state anxiety scores. At the end of 8 weeks, both groups demonstrated enhanced psychological functions, but the experimental group receiving additional yoga breathing performed better than the group practicing yoga alone.

**Conclusion:** An additional practice of yoga breathing with intermittent breath holding was found to enhance the psychological functions in young adult yoga practitioners.


**Abstract:**

**Background:** Acute gastroenteritis in children accounts for about 10% of hospital admissions and is still one of the major causes of death worldwide. As many children are treated with complementary and alternative medicine (CAM) and anthroposophic medicine, respectively, especially in Europe, the aim of this review was to descriptively present published anthroposophic therapies
applied for the treatment of acute gastroenteritis in childhood.

**Methods:** A complex search strategy recording a broad spectrum of CAM therapies was developed to identify anthroposophic therapy options for the treatment of gastroenteritis in children. The search was conducted in 4 general scientific as well as 3 CAM-specific databases.

**Results:** In total, 3,086 articles were identified and screened for anthroposophic related content. The majority of hits deal with nutritional/dietary therapies. Articles considering anthroposophic approaches constitute only 3.1% (7/227) of all CAM-related articles. Among these articles 2 observational studies, 3 experience reports and 2 reviews were identified. In the experience reports, a variety of anthroposophic remedies was recommended but mostly unsupported by scientific evidence. However, observational studies for the anthroposophic medications, Bolus alba comp. and Gentiana comp., were detected. Additionally, studies investigating the efficacy and safety of Chamomilla, Ipecacuanha, Podophyllum or Tormentilla preparations in homeopathy and phytomedicine, respectively, were presented.

**Conclusions:** Most CAM-associated therapies for gastroenteritis in childhood comprise dietary recommendations. Studies concerning anthroposophic approaches and medications, respectively, are deficient. The results of this study underline that effort is needed to evaluate anthroposophic therapies in a clinical setting.


**Abstract:**

**Introduction:** Analysis of data derived from homeopathic pathogenetic trials (HPTs, homeopathic drug provings) has been a challenge. Most parts of the homeopathic pharmacopeia were sourced from Hahnemann’s Materia Medica Pura (1825–1833), TF Allen’s Encyclopedia (1874) and Constantine Hering's Materia Medica (1879–1891), well before randomised controlled trials were in use. As a result, such studies and their outcomes harbour a large risk of inclusion of unreliable symptoms.

**Aims and Objective:** The main purpose of this article is to introduce Quantitative and Qualitative Pathogenetic Indices to improve the method of analysis of symptoms.

**Materials and Methods:** The data from HPTs for human immunodeficiency virus nosode, hepatitis C nosode, capsaicin alkaloids (capsaicin and dihydrocapsaicin) and hydroquinone (HQ) were extracted and analysed in terms of novel Qualitative and Quantitative Pathogenetic Indices. Taken into the consideration were the qualitative aspect of a symptom (i.e. its intensity), and the quantitative aspect by calculating the number of symptoms per
volunteer per day. The pathogenetic effects and data evaluation indices were calculated for each HPT. A comparison was made of symptoms of verum versus placebo provers in terms of their quantity and quality.

**Results:** Four HPTs involving 81 volunteers (56 on verum and 25 on placebo) generated 555 symptoms or pathogenetic effects (excluding run-in phase symptoms), of which 448 (81%) were reported by volunteers who were in the verum arm, and 107 (19%) were reported by volunteers on placebo. The overall mean incidence of pathogenetic effects for the four HPTs was thus 8 per verum prover and 4.28 per placebo prover. The corresponding mean Quantitative Pathogenetic Index was 0.23 symptoms per volunteer per day for the verum arm and 0.12 symptoms per volunteer per day for the placebo arm. The overall mean incidence of pathogenetic effects in the run-in phase was less. The overall mean Qualitative Pathogenetic Index (number of symptoms, of a given intensity, per volunteer per day) for the verum arm was 0.09 versus 0.05 for the placebo arm.

**Conclusion:** The symptoms exhibited by volunteers in the verum arm were more numerous and more intense than those in the placebo arm. An innovative and logical method of reporting of symptoms and analysis has been introduced by the use of these pathogenetic indices, which can be used in future as measurement tools for analysis of data from HPTs.


**Abstract:**

HIV-AIDS is an epidemic that causes an excessive load on the health care system. In the last decade, HIV has erupted worldwide. Homeopathy holds the potential for improving patients’ well-being and prolonging life by ameliorating the draining side effects of antiretro viral (ARV) drugs. This article attempts to bridge the gap between homeopathic and conventional therapeutic plans. The author has cited a case from a clinical setting where a patient discontinued ARV drugs, and consulted a homeopath for herpes zoster infection. The patient was followed up for 1 year, was relieved from symptoms and remained free from opportunistic infections. Homeopathy helped him; he regained confidence in himself and the homeopathic therapeutic measures. The case illustrated here, which has shown improvement in both subjective and objective parameters, may be used for the management of patients suffering from HIV or AIDS.


Abstract:

**Background:** To determine if Kava Kava is an effective treatment for combating symptoms of anxiety despite warnings of hepatotoxicity from the Centers for Disease Control and Prevention (CDC).

**Methods:** Databases PubMed, CINAHL, and PsycINFO were utilized to obtain clinical trials on Kava Kava and its effects on anxiety. A total of 11 articles met inclusion/exclusion criteria: 2 for Kava Kava vs. another anti-anxiety medication, 2 detailing additional adverse events, and 7 for Kava Kava vs. placebo. Mantel-Haenszel fixed-effects model was used to analyze the data, with responder rates being pooled to compute weighted risk ratios.

**Results:** Kava Kava was shown to be more effective than placebo in 3 of the 7 trials. A final risk ratio of 1.50 (95% CI: 1.12, 2.01) from responder rates was calculated in favor of the intervention from 5 clinical trials (n = 330). Adverse events were shown to be the same as placebo (P = 0.574), and laboratory values analyzing hepatotoxicity were no different when compared to baseline except in two studies.

**Conclusions:** Kava Kava appears to be a short-term treatment for anxiety, but not a replacement for prolonged anti-anxiety use. Although not witnessed in this review, liver toxicity is especially possible if taken longer than 8 weeks.


Abstract:

**Background and purpose:** This study examines the relationship between the use of complementary medicine (CM) interventions or consultations with CM practitioners and women's choice of contraceptive method.

**Materials and methods:** A secondary analysis of a cross-sectional survey of Australian Women aged 34–39 years from the Australian Longitudinal Study on Women's Health (ALSWH) was conducted. Associations between use of CM and contraception were analysed using Chi-squared tests and multivariate logistic regression.

**Results:** Based on the responses from the included women (n = 7299), women who consulted a naturopath/herbalist were less likely to use implant contraceptives (OR 0.56; 95% confidence interval (CI) 0.33; 0.95). Those
consulting a chiropractor (OR 1.54; 95%CI 1.05; 2.25) or an osteopath (OR 2.16; 95% CI 1.32; 3.54) were more likely to use natural contraception.

**Conclusion:** There may be a link between women's choice of contraceptive method and their use of CM, in particular, with CM practitioner consultations.


**Thokchom Suresh Kumar, Gulati Kavita, Ray Arunabha et al. Effects of yogic intervention on pulmonary functions and health status in patients of COPD and the possible mechanisms. Complementary Therapies in Clinical Practice 2018; (33): 20-26p.**

**Vieira Andreia, Reis Ana Mafalda, Matos Luís Carlos et al. Does auriculotherapy have therapeutic effectiveness? An overview of systematic reviews. Complementary Therapies in Clinical Practice 2018; (33): 61-70p.**

**Abstract:**

**Background and purpose:** Auriculotherapy is a therapeutic technique used for a wide variety of conditions. Nevertheless, similarly to any health related intervention, the clinical use of this therapy requires scientific evidence of effectiveness in order to support its rational use. The main goal of this article is to critically analyze published literature on auriculotherapy and to provide an overview of the effectiveness of this technique in the management of health disorders.

**Methods:** The inventory of published reviews on this subject was carried out in November 2017, by assessing the following computerized databases: PubMed, MEDLINE, PsycINFO, EBMR, Cochrane Database of Systematic Reviews, CINAHL Plus NRC and Science Direct. Were only considered the systematic reviews based on meta-analysis with high methodological quality described according to AMSTAR (Assessment of Multiple Systematic Reviews). The eligible articles were systematically reviewed to find out in which health conditions auriculotherapy can be used with effectiveness.

**Results:** A total of 14 reviews were eligible according to the inclusion and exclusion criterions. Those reviews were focused on the management of insomnia, smoking cessation and pain, within the clinical scope of Neurology, Orthopaedics and Rheumatology.
**Conclusions:** Auriculotherapy has shown to have positive effects while associated to conventional treatments of insomnia, chronic and acute pain. Further well designed studies are required to evaluate the effectiveness of this technique in the treatment of other health conditions.


**Abstract:**
Informal caregivers of allogeneic hematopoietic cell transplant patients experience significant levels of stress throughout the caregiving process. One strategy that has been shown to aid in stress management in other populations is mindfulness. The goal of this study was to understand caregivers' experiences with mindfulness and evaluate their receptiveness to a mindfulness-based stress management program. Data were collected via in-depth phone interviews from 18 caregivers (55% female). Results indicated that about half the sample was familiar with mindfulness and/or had practiced meditation. The majority indicated that they believed a mindfulness program would have been useful for them and that they would have been willing to participate. Most indicated that a program delivered once-weekly for 60 min, during both inpatient and outpatient phases, would be preferable through a combination of in-person and mobile-based delivery. These data provide critical information for the development of future mindfulness-based interventions for this caregiving population.


**Abstract:**
Obsessive-compulsive disorder (OCD) is a chronic serious anxiety disorder affecting as many as 1.2% of the population worldwide. A female diagnosed with OCD was brought by her family for homeopathic treatment and with the help of Constantine Hering’s ‘Analytical Repertory of the Symptoms of the Mind’ and Boger’s ‘Boeninghausen’s Characteristics and Repertory’, the remedy Sulphur was chosen. A single dose of 30th potency helped the patient recover gradually over 2 months and she continues to lead a drug-free normal life over one and a half years of follow-up.


**Abstract:**
**Context:** Throughout history people have reported exceptional experiences that appear to transcend the everyday boundaries of space and time, such as perceiving someone’s thoughts from a distance. Because such experiences are associated with superstition, and some violate currently accepted materialist conventions, one might assume that scientists and engineers would be much less likely to report instances of these experiences than the general population.

**Objectives:** To evaluate 1) the prevalence of exceptional human experiences (EHEs), 2) the level of paranormal belief, 3) the relationship between them, and 4) potential predictors of EHEs in three groups.

**Participants:** Potential volunteers were randomly selected to receive invitations for an anonymous survey.

**Main Measures:** Data were collected on 25 different types of EHEs, demographics, religious or spiritual affiliations, paranormal beliefs, mental health, and personality traits. Group differences were analyzed with chi-square tests and analysis of variance, and predictors were evaluated with a general linear model.

**Results:** 94.0% of the general population (n = 283), 93.2% of scientists and engineers (n = 175), and 99.3% of enthusiasts (n = 441) endorsed at least one EHE ($X^2(2) = 21.1, p < 0.0005$). Paranormal belief was highest in EHE enthusiasts, followed by scientists and the general population ($F(2,769) = 116.2, p < 0.0005$). Belief was positively correlated with experience ($r = 0.61, p < 0.0005$). An exploratory general linear model showed that variables such as mental health, personality, impact and family history predict the endorsement and frequency of EHEs. This study indicates that EHEs occur frequently in both the general population and in scientists and engineers.


**Abstract:**

**Objectives:** Research suggests Animal Assisted Interventions (AAI) reduce negative outcomes in medical settings, but quantitative examinations of their effects on medical outcomes such as pain, anxiety, and distress are lacking.

**Design:** A comprehensive literature search and meta-analysis were conducted in which 22 studies (13 child, 9 adult) met inclusion criteria. Both intervention versus control and intervention pre-post effect sizes were computed using a random effects model.
Results: The overall intervention versus control effect size was large and significant ($d = 1.65$, 95% CI $= 0.46–2.832$). Similarly, the pre-post effect size was large and significant ($d = 2.19$, 95% CI $= 0.74–3.64$).

Conclusions: The results of this meta-analysis indicate that AAI can yield large effects across a number of medically relevant outcomes. There is, however, substantial methodological variation across studies and more randomized clinical trials with stronger methodological controls are needed to establish the effectiveness of AAI compared to other interventions.


Abstract:
**Background and purpose:** Chinese medicine is increasingly used by women with postpartum depression (PPD). We systematically analyzed randomized controlled trials of acupuncture and Chinese herbal medicine (CHM) for PPD.

**Methods:** Studies were retrieved from English and Chinese databases. The Cochrane risk of bias tool was used to assess methodological quality.

**Results:** Fifteen CHM, and three acupuncture studies were included. Low quality evidence suggested that CHM alone or combined with antidepressants as add-on therapy may reduce symptoms of depression compared to placebo or antidepressants on the Edinburgh Postnatal Depression Scale (EPDS). There was no statistically significant difference between acupuncture and antidepressants. Adverse events were rare.

**Conclusions:** CHM reduced PPD symptoms greater than placebo or antidepressants. Acupuncture was neither superior nor inferior to antidepressants. More rigorously designed studies are required to confirm the effect of CHM and acupuncture for PPD.


**Abstract:**

**Background and purpose:** Patients on hemodialysis experience anxiety and depression. This study aimed to investigate the effect of guided imagery on anxiety, depression, and vital signs in patients on hemodialysis.

**Materials and methods:** This randomized controlled clinical trial was conducted on 80 patients undergoing hemodialysis. The subjects were randomly assigned into two groups: a guided intervention group and a control group. Anxiety and depression were measured using the Hospital Anxiety and Depression Scale.

**Results:** After the intervention, the level of anxiety and depression were significantly lower in the intervention group compared with the control group (p = 0.030, p = 0.001, respectively). A statistically significant reduction in the respiratory rate and heart rate was reported in the intervention group (p < 0.05).
Conclusion: Nurses are suggested to use guided imagery along with other interventions for the management of anxiety and depression. It can alleviate adverse psychological responses among patients on hemodialysis.


Abstract:

Introduction: Systematic reviews need constantly updating as new evidence emerges. The aim of this comprehensive systematic review/meta-analysis focused on trials that provided acupuncture during in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) which were compared with routine care for a range of outcomes - implantation rate, biochemical pregnancies (presence of a positive urinary pregnancy test or a positive serum human chorionic gonadotrophin test), clinical pregnancies, ongoing pregnancies, and rates of miscarriage and live birth.

Methods: A systematic search of MEDLINE and EMBASE databases for randomized controlled trials (RCTs) on acupuncture treatment during IVF or ICSI was carried out from database inception until July 31, 2017. Study selection, data extraction, quality assessment and bias assessment were carried out by 2 researchers independently, with adjudication by the third researcher when necessary. A meta-analysis was performed to compare outcomes between women receiving acupuncture and those receiving routine care, and pooled relative risks (RR) were calculated.

Results: Statistically significant differences were observed in rates of clinical pregnancy (RR = 1.19, 95% confidence intervals (CI): 1.06–1.34 p = 0.002), live birth (RR = 1.36, 95% CI: 1.09–1.69 p = 0.006), and implantation rate (RR = 1.31, 95% CI: 1.08–1.59 p = 0.006) between the acupuncture and the control groups. No significant differences were found for biochemical pregnancies (RR = 1.12, 95% CI: 0.92–1.35 p = 0.268), ongoing pregnancies (RR = 1.21, 95% CI: 0.95–1.55 p = 0.130), or miscarriage (RR = 0.89, 95% CI: 0.67–1.20 p = 0.447) between the two groups. Adverse events were described in 4 studies.

Conclusions: Acupuncture may have an impact on the outcome rates of implantation, clinical pregnancy, and live birth; however, well-designed RCTs are warranted to further validate its effects.
Allied System


Abstract:

**Background:** Arthroscopic partial meniscectomy is one of the most common orthopaedic procedures worldwide. Clinical trial evidence published in the past 6 years, however, has raised questions about the effectiveness of the procedure in some patient groups. In view of concerns about potential overuse, we aimed to establish the true risk of serious complications after arthroscopic partial meniscectomy.

**Methods:** We analysed national Hospital Episode Statistics data for all arthroscopic partial meniscectomies done in England between April 1, 1997, and March 31, 2017. Simultaneous or staged (within 6 months) bilateral cases were excluded. We identified complications occurring in the 90 days after the index procedure. The primary outcome was the occurrence of at least one serious complication within 90 days, which was defined as either myocardial infarction, stroke, pulmonary embolism, infection requiring surgery, fasciotomy, neurovascular injury, or death. Logistic regression
modelling was used to identify factors associated with complications and, when possible, risk was compared with general population data.

**Findings:** During the study period 1,088,782 arthroscopic partial meniscectomies were done, 699,965 of which were eligible for analysis. Within 90 days, serious complications occurred in 2,218 (0.317% [95% CI 0.304–0.330]) cases, including 546 pulmonary embolisms (0.078% [95% CI 0.072–0.085]) and 944 infections necessitating further surgery (0.135% [95% CI 0.126–0.144]). Increasing age (adjusted odds ratio [OR] 1.247 per decade [95% CI 1.208–1.288]) and modified Charlson comorbidity index (adjusted OR 1.860 per 10 units [95% CI 1.708–2.042]) were associated with an increased risk of serious complications. Female sex was associated with a reduced risk of serious complications (adjusted OR 0.640 [95% CI 0.580–0.705]). The risk of mortality fell over time (adjusted OR 0.965 per year [95% CI 0.937–0.994]). Mortality, myocardial infarction, and stroke occurred less frequently in the study cohort than in the general population. The risks of infection and pulmonary embolism did not change during the study, and were significantly higher in the study cohort than in the general population. For every 1,390 (95% CI 1,272–1,532) fewer knee arthroscopies done, one pulmonary embolism could be prevented. For every 749 (95% CI 704–801) fewer procedures done, one native knee joint infection could be prevented.

**Interpretation:** Overall, the risk associated with undergoing arthroscopic partial meniscectomy was low. However, some rare but serious complications (including pulmonary embolism and infection) are associated with the procedure, and the risks have not fallen with time. In view of uncertainty about the effectiveness of arthroscopic partial meniscectomy, an appreciation of relative risks is crucial for patients and clinicians. Our data provide a basis for decision making and consent.

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


**Abstract:**

Will the Sustainable Development Goal 3 sub-goal “Achieve universal health coverage, including financial risk protection, access to quality essential health care services and...safe, effective, quality and affordable essential medicines and vaccines for all” be judged a breakthrough or a great white elephant in implementation, when we look back with the clear eyes of hindsight in 2030? What are the ways in which this agenda might play out in implementation and why might it do so? Drawing on a desk review, this Essay explores dominant ideas, ideology, institutions, and interests in relation to global versus Ghana national health priorities since the WHO constitution came into effect in 1948, to reflect on these questions.


Abstract:

**Background:** There is a direct relationship between bodyweight and risk of diabetes. Lorcaserin, a selective serotonin 2C receptor agonist that suppresses appetite, has been shown to facilitate sustained weight loss in obese or overweight patients. We aimed to evaluate the long-term effects of lorcaserin on diabetes prevention and remission.

**Methods:** In this randomised, double-blind, placebo-controlled trial done in eight countries, we recruited overweight or obese patients (body-mass index ≥27 kg/m2) with or at high risk for atherosclerotic vascular disease. Eligible patients were aged 40 years or older; patients at high risk for atherosclerotic vascular disease had to be aged 50 years or older with diabetes and at least one other risk factor. Patients were randomly assigned to receive either lorcaserin (10 mg twice daily) or matching placebo. Additionally, all patients had access to a standardised weight management programme based on lifestyle modification. The prespecified primary metabolic efficacy endpoint of time to incident diabetes was assessed in patients with prediabetes at baseline. The prespecified secondary outcomes for efficacy were incident diabetes in all patients without diabetes, achievement of normoglycaemia in patients with prediabetes, and change in glycated haemoglobin (HbA1c) in patients with diabetes. Hypoglycaemia was a prespecified safety outcome. Analysis was by intention to treat, using Cox proportional hazard models for time-to-event analyses. This trial is registered with ClinicalTrials.gov, number NCT02019264.

**Findings:** Between Feb 7, 2014, and Nov 20, 2015, 12 000 patients were randomly assigned to lorcaserin or placebo (6000 patients in each group) and followed up for a median of 3·3 years (IQR 3·0–3·5). At baseline, 6816 patients (56·8%) had diabetes, 3991 (33·3%) prediabetes, and 1193 (9·9%) normoglycaemia. At 1 year, patients treated with lorcaserin had a net weight loss beyond placebo of 2·6 kg (95% CI 2·3–2·9) for those with diabetes, 2·8 kg (2·5–3·2) for those with prediabetes, and 3·3 kg (2·6–4·0) for those with normoglycaemia (p<0·0001 for all analyses). Lorcaserin reduced the risk of incident diabetes by 19% in patients with prediabetes (172 [8·5%] of 2015 vs 204 [10·3%] of 1976; hazard ratio 0·81, 95% CI 0·66–0·99; p=0·038) and by 23% in patients without diabetes (174 [6·7%] of 2615 vs 215 [8·4%] of 2569; 0·77, 0·63–0·94; p=0·012). Lorcaserin resulted in a non-significant increase in the rate of achievement of normoglycaemia in patients with prediabetes (185 [9·2%] vs 151 [7·6%]; 1·20, 0·97–1·49; p=0·093). In patients with diabetes, lorcaserin resulted in a reduction of 0·33% (95% CI 0·29–0·38; p<0·0001) in HbA1c compared with placebo at 1 year from a mean baseline of 53 mmol/mol (7·0%). In patients with diabetes at baseline, severe
hypoglycaemia with serious complications was rare, but more common with lorcaserin (12 [0·4%] vs four [0·1%] events; p=0·054).

**Interpretation:** Lorcaserin decreases risk for incident diabetes, induces remission of hypoglycaemia, and reduces the risk of microvascular complications in obese and overweight patients, supporting the role of lorcaserin as an adjunct to lifestyle modification for chronic management of weight and metabolic health.

**Funding:** Eisai.


**Abstract:**

**Background:** Non-contrast head CT scan is the current standard for initial imaging of patients with head trauma or stroke symptoms. We aimed to develop and validate a set of deep learning algorithms for automated detection of the following key findings from these scans: intracranial haemorrhage and its types (ie, intraparenchymal, intraventricular, subdural, extradural, and subarachnoid); calvarial fractures; midline shift; and mass effect.

**Methods:** We retrospectively collected a dataset containing 313 318 head CT scans together with their clinical reports from around 20 centres in India between Jan 1, 2011, and June 1, 2017. A randomly selected part of this dataset (Qure25k dataset) was used for validation and the rest was used to develop algorithms. An additional validation dataset (CQ500 dataset) was collected in two batches from centres that were different from those used for the development and Qure25k datasets. We excluded postoperative scans and scans of patients younger than 7 years. The original clinical radiology report and consensus of three independent radiologists were considered as gold standard for the Qure25k and CQ500 datasets, respectively. Areas under the receiver operating characteristic curves (AUCs) were primarily used to assess the algorithms.

**Findings:** The Qure25k dataset contained 21 095 scans (mean age 43 years; 9030 [43%] female patients), and the CQ500 dataset consisted of 214 scans in the first batch (mean age 43 years; 94 [44%] female patients) and 277 scans in the second batch (mean age 52 years; 84 [30%] female patients). On the Qure25k dataset, the algorithms achieved an AUC of 0·92 (95% CI 0·91–0·93) for detecting intracranial haemorrhage (0·90 [0·89–0·91] for intraparenchymal, 0·96 [0·94–0·97] for intraventricular, 0·92 [0·90–0·93] for
subdural, 0·93 [0·91–0·95] for extradural, and 0·90 [0·89–0·92] for subarachnoid). On the CQ500 dataset, AUC was 0·94 (0·92–0·97) for intracranial haemorrhage (0·95 [0·93–0·98], 0·93 [0·87–1·00], 0·95 [0·91–0·99], 0·97 [0·91–1·00], and 0·96 [0·92–0·99], respectively). AUCs on the Qure25k dataset were 0·92 (0·91–0·94) for calvarial fractures, 0·93 (0·91–0·98), 0·95 [0·91–0·99], 0·97 [0·91–1·00], and 0·96 [0·92–0·99], respectively. AUCs on the CQ500 dataset were 0·96 (0·92–1·00), 0·97 (0·94–1·00), and 0·92 (0·89–0·95), respectively.

**Interpretation:** Our results show that deep learning algorithms can accurately identify head CT scan abnormalities requiring urgent attention, opening up the possibility to use these algorithms to automate the triage process.

**Funding:** Qure.ai.

**Dehghan Mahshid, Mente Andrew, Rangarajan Sumathy et al.**

**Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): A prospective cohort study.**


**Abstract:**

**Background:** Dietary guidelines recommend minimising consumption of whole-fat dairy products, as they are a source of saturated fats and presumed to adversely affect blood lipids and increase cardiovascular disease and mortality. Evidence for this contention is sparse and few data for the effects of dairy consumption on health are available from low-income and middle-income countries. Therefore, we aimed to assess the associations between total dairy and specific types of dairy products with mortality and major cardiovascular disease.

**Methods:** The Prospective Urban Rural Epidemiology (PURE) study is a large multinational cohort study of individuals aged 35–70 years enrolled from 21 countries in five continents. Dietary intakes of dairy products for 136 384 individuals were recorded using country-specific validated food frequency questionnaires. Dairy products comprised milk, yoghurt, and cheese. We further grouped these foods into whole-fat and low-fat dairy. The primary outcome was the composite of mortality or major cardiovascular events (defined as death from cardiovascular causes, non-fatal myocardial infarction, stroke, or heart failure). Hazard ratios (HRs) were calculated using multivariable Cox frailty models with random intercepts to account for clustering of participants by centre.
Findings: Between Jan 1, 2003, and July 14, 2018, we recorded 10,567 composite events (deaths [n=6796] or major cardiovascular events [n=5855]) during the 9.1 years of follow-up. Higher intake of total dairy (>2 servings per day compared with no intake) was associated with a lower risk of the composite outcome (HR 0.84, 95% CI 0.75–0.94; \( p_{\text{trend}} = 0.0004 \)), total mortality (0.83, 0.72–0.96; \( p_{\text{trend}} = 0.0052 \)), non-cardiovascular mortality (0.86, 0.72–1.02; \( p_{\text{trend}} = 0.046 \)), cardiovascular mortality (0.77, 0.58–1.01; \( p_{\text{trend}} = 0.029 \)), major cardiovascular disease (0.78, 0.67–0.90; \( p_{\text{trend}} = 0.0001 \)), and stroke (0.66, 0.53–0.82; \( p_{\text{trend}} = 0.0003 \)). No significant association with myocardial infarction was observed (HR 0.89, 95% CI 0.71–1.11; \( p_{\text{trend}} = 0.163 \)). Higher intake (>1 serving vs no intake) of milk (HR 0.90, 95% CI 0.82–0.99; \( p_{\text{trend}} = 0.0529 \)) and yogurt (0.86, 0.75–0.99; \( p_{\text{trend}} = 0.0051 \)) was associated with lower risk of the composite outcome, whereas cheese intake was not significantly associated with the composite outcome (0.88, 0.76–1.02; \( p_{\text{trend}} = 0.1399 \)). Butter intake was low and was not significantly associated with clinical outcomes (HR 1.09, 95% CI 0.90–1.33; \( p_{\text{trend}} = 0.4113 \)).

Interpretation: Dairy consumption was associated with lower risk of mortality and major cardiovascular disease events in a diverse multinational cohort.

Funding: Full funding sources are listed at the end of the paper (see Acknowledgments).


Abstract:

With the global increase in ageing populations, a current and future key challenge is to improve health expectancy. It is well established that normal ageing is associated with a loss of muscle mass (sarcopenia), with concomitant loss of muscle function and increased risk of falls, reduced ability to perform daily tasks and subsequent reduced quality of life. Therefore, a balanced and optimal protein-energy homeostasis is recognised
as a major dietary-related determinant of healthy ageing. This short article provides an overview of the current evidence relating to protein intake in older adults.

Older adults may benefit from a protein intake above the recommended daily allowance, with an intake of ≥1.2 g/kg/day to help prevent age-related sarcopenia. The failure of older people to adequately regulate food and nutrient intake results in weight loss, and such changes have been termed the anorexia of ageing and have been attributed to multiple factors affecting the satiety cascade. The quality and timing of protein supplementation in addition to quantity is very important. To improve muscle protein synthesis, pulse feeding may be more effective than bolus feeding, but further evidence is needed. Key foci of ongoing research should be to provide robust evidence from trials in older adults to help define the optimum type and timing of dietary protein supplements.


Abstract:

Background: LY3298176 is a novel dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist that is being developed for the treatment of type 2 diabetes. We aimed to examine the efficacy and safety of co-stimulation of the GLP-1 and GIP receptors with LY3298176 compared with placebo or selective stimulation of GLP-1 receptors with dulaglutide in patients with poorly controlled type 2 diabetes.

Methods: In this double-blind, randomised, phase 2 study, patients with type 2 diabetes were randomly assigned (1:1:1:1:1:1) to receive either once-weekly subcutaneous LY3298176 (1 mg, 5 mg, 10 mg, or 15 mg), dulaglutide (1·5 mg), or placebo for 26 weeks. Assignment was stratified by baseline glycated haemoglobin A1c (HbA1c), metformin use, and body-mass index (BMI). Eligible participants (aged 18–75) had type 2 diabetes for at least 6 months (HbA1c 7·0–10·5%, inclusive), that was inadequately controlled with diet and exercise alone or with stable metformin therapy, and a BMI of 23–50 kg/m2. The primary efficacy outcome was change in HbA1c from baseline to 26 weeks in the modified intention-to-treat (mITT) population (all patients who received at least one dose of study drug and had at least one postbaseline measurement of any outcome). Secondary endpoints, measured in the mITT on treatment dataset, were change in HbA1c from baseline to 12 weeks; change in mean bodyweight, fasting plasma glucose, waist circumference, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides, and proportion of patients reaching the HbA1c target (≤6·5% and <7·0%) from
baseline to weeks 12 and 26; and proportion of patients with at least 5% and 10% bodyweight loss from baseline to 26 weeks. This study is registered with ClinicalTrials.gov, number NCT03131687.

Findings: Between May 24, 2017, and March 28, 2018, 555 participants were assessed for eligibility, of whom 318 were randomly assigned to one of the six treatment groups. Because two participants did not receive treatment, the modified intention-to-treat and safety populations included 316 participants. 258 (81·7%) participants completed 26 weeks of treatment, and 283 (89·6%) completed the study. At baseline, mean age was 57 years (SD 9), BMI was 32·6 kg/m² (5·9), duration from diagnosis of diabetes was 9 years (6), HbA1c was 8·1% (1·0), 53% of patients were men, and 47% were women.

At 26 weeks, the effect of LY3298176 on change in HbA1c was dose-dependent and did not plateau. Mean changes from baseline in HbA1c with LY3298176 were −1·06% for 1 mg, −1·73% for 5 mg, −1·89% for 10 mg, and −1·94% for 15 mg, compared with −0·06% for placebo (posterior mean differences [80% credible set] vs placebo: −1·00% [−1·22 to −0·79] for 1 mg, −1·67% [−1·88 to −1·46] for 5 mg, −1·83% [−2·04 to −1·61] for 10 mg, and −1·89% [−2·11 to −1·67] for 15 mg). Compared with dulaglutide (−1·21%) the posterior mean differences (80% credible set) for change in HbA1c from baseline to 26 weeks with the LY3298176 doses were 0·15% (−0·08 to 0·38) for 1 mg, −0·52% (−0·72 to −0·31) for 5 mg, −0·67% (−0·89 to −0·46) for 10 mg, and −0·73% (−0·95 to −0·52) for 15 mg. At 26 weeks, 33–90% of patients treated with LY3298176 achieved the HbA1c target of less than 7·0% (vs 52% with dulaglutide, 12% with placebo) and 15–82% achieved the HbA1c target of at least 6·5% (vs 39% with dulaglutide, 2% with placebo). Changes in fasting plasma glucose ranged from −0·4 mmol/L to −3·4 mmol/L for LY3298176 (vs 0·9 mmol/L for placebo, −1·2 mmol/L for dulaglutide). Changes in mean bodyweight ranged from −0·9 kg to −11·3 kg for LY3298176 (vs −0·4 kg for placebo, −2·7 kg for dulaglutide). At 26 weeks, 14–71% of those treated with LY3298176 achieved the weight loss target of at least 5% (vs 22% with dulaglutide, 0% with placebo) and 6–39% achieved the weight loss target of at least 10% (vs 9% with dulaglutide, 0% with placebo). Changes in waist circumference ranged from −2·1 cm to −10·2 cm for LY3298176 (vs −1·2 cm for placebo, −2·5 cm for dulaglutide). Changes in total cholesterol ranged from 0·2 mmol/L to −0·3 mmol/L for LY3298176 (vs 0·3 mmol/L for placebo, −0·2 mmol/L for dulaglutide). Changes in HDL or LDL cholesterol did not differ between the LY3298176 and placebo groups. Changes in triglyceride concentration ranged from 0 mmol/L to −0·8 mmol/L for LY3298176 (vs 0·3 mmol/L for placebo, −0·3 mmol/L for dulaglutide). The 12-week outcomes were similar to those at 26 weeks for all secondary outcomes. 13 (4%) of 316 participants across the six treatment groups had 23 serious adverse events in total. Gastrointestinal events (nausea, diarrhoea, and vomiting) were the most common treatment-emergent adverse events. The incidence of gastrointestinal events was dose-related (23·1% for 1 mg LY3298176, 32·7% for 5 mg LY3298176, 51·0% for 10 mg LY3298176, and 66·0% for 15 mg LY3298176, 42·6% for dulaglutide, 9·8% for placebo); most events were mild to moderate in intensity and transient. Decreased appetite was the second
most common adverse event (3.8% for 1 mg LY3298176, 20.0% for 5 mg LY3298176, 25.5% for 10 mg LY3298176, 18.9% for 15 mg LY3298176, 5.6% for dulaglutide, 2.0% for placebo). There were no reports of severe hypoglycaemia. One patient in the placebo group died from lung adenocarcinoma stage IV, which was unrelated to study treatment.

**Interpretation:** The dual GIP and GLP-1 receptor agonist, LY3298176, showed significantly better efficacy with regard to glucose control and weight loss than did dulaglutide, with an acceptable safety and tolerability profile. Combined GIP and GLP-1 receptor stimulation might offer a new therapeutic option in the treatment of type 2 diabetes.

**Funding:** Eli Lilly and Company.


**Abstract:**

**Background:** At present, biological disease-modifying anti-rheumatic drugs (DMARDs) are the only treatment recommended for patients with ankylosing spondylitis who have not responded to first-line treatment with non-steroidal anti-inflammatory drugs (NSAIDs). The TORTUGA trial investigated the efficacy and safety of filgotinib, an oral selective Janus kinase 1 (JAK1) inhibitor, for the treatment of patients with active ankylosing spondylitis.

**Methods:** In this completed, randomised, double-blind, placebo-controlled, phase 2 trial, we enrolled adult patients from 30 sites in seven countries (Belgium, Bulgaria, Czech Republic, Estonia, Poland, Spain, and Ukraine). Eligible patients had active ankylosing spondylitis and an inadequate response or intolerance to two or more NSAIDs. Patients were randomly assigned (1:1) with an interactive web-based response system to receive filgotinib 200 mg or placebo orally once daily for 12 weeks. Randomisation was stratified by current use of conventional synthetic DMARDs and previous receipt of anti-tumour necrosis factor therapy. The patients, study team, and study sponsor were masked to treatment assignment. The primary endpoint was the change from baseline in ankylosing spondylitis disease activity score (ASDAS) at week 12, which was assessed in the full analysis set (ie, all randomised patients who received at least one dose of study drug). Safety was assessed according to actual treatment received. This trial is registered with ClinicalTrials.gov, number NCT03117270.

**Findings:** Between March 7, 2017, and July 2, 2018, 263 patients were screened and 116 randomly assigned to filgotinib (n=58) or placebo (n=58). 55 (95%) patients in the filgotinib group and 52 (90%) in the placebo group completed the study; three (5%) patients in the filgotinib group and six (10%) in the placebo group discontinued treatment. The mean ASDAS change from baseline to week 12 was −1.47 (SD 1.04) in the filgotinib group and −0.57
(0·82) in the placebo group, with a least squares mean difference between groups of −0·85 (95% CI −1·17 to −0·53; p<0·0001). Treatment-emergent adverse events were reported in 18 patients in each group, the most common being nasopharyngitis (in two patients in the filgotinib group and in four patients in the placebo group). Treatment-emergent adverse events led to permanent treatment discontinuation in two patients (a case of grade 3 pneumonia in the filgotinib group and of high creatine kinase in the placebo group). No deaths were reported during the study.

**Interpretation:** Filgotinib is efficacious and safe for the treatment of patients with active ankylosing spondylitis who have not responded to first-line pharmacological therapy with NSAIDs. Further investigation of filgotinib for ankylosing spondylitis is warranted.

**Funding:** Galapagos and Gilead Sciences.

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**Kruk Margaret E, Gage Anna D, Joseph Naima T et al. Mortality due to low-quality health systems in the universal health coverage era: A Systematic analysis of amenable deaths in 137 countries. Lancet 2018; 392(10160): 2203-12p.**

**Abstract:**

**Background:** Universal health coverage has been proposed as a strategy to improve health in low-income and middle-income countries (LMICs). However, this is contingent on the provision of good-quality health care. We estimate the excess mortality for conditions targeted in the Sustainable Development Goals (SDG) that are amenable to health care and the portion of this excess mortality due to poor-quality care in 137 LMICs, in which excess mortality refers to deaths that could have been averted in settings with strong health systems.

**Methods:** Using data from the 2016 Global Burden of Disease study, we calculated mortality amenable to personal health care for 61 SDG conditions by comparing case fatality between each LMIC with corresponding numbers from 23 high-income reference countries with strong health systems. We used data on health-care utilisation from population surveys to separately estimate the portion of amenable mortality attributable to non-utilisation of health care versus that attributable to receipt of poor-quality care.

**Findings:** 15·6 million excess deaths from 61 conditions occurred in LMICs in 2016. After excluding deaths that could be prevented through public health measures, 8·6 million excess deaths were amenable to health care of which 5·0 million were estimated to be due to receipt of poor-quality care and 3·6 million were due to non-utilisation of health care. Poor quality of health
care was a major driver of excess mortality across conditions, from cardiovascular disease and injuries to neonatal and communicable disorders.

**Interpretation:** Universal health coverage for SDG conditions could avert 8.6 million deaths per year but only if expansion of service coverage is accompanied by investments into high-quality health systems.

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

**Kwon Chan Young, Lee Boram, Lee Ju Ah. Efficacy and safety of bloodletting on ear apex for primary hypertension: A systematic review and meta-analysis.** European Journal of Integrative Medicine 2018; 23: 90-100p.

**Abstract:**

**Introduction:** Conventional pharmacotherapy on hypertension has some issues including its side effects, resistant hypertension, withdrawal, and polypharmacy. Bloodletting on ear apex (BEA) is a non-pharmacological treatment known to be useful in lowering high blood pressure in oriental medicine. This study was conducted to explore the evidence base to investigate whether this technique could help in the treatment of hypertension.

**Methods:** We conducted a systematic review and meta-analysis for randomized controlled trials (RCTs) evaluating the antihypertensive effect of BEA. The methodological quality of included studies was assessed by using Cochrane Collaboration’s risk of bias tool.

**Results:** Eight RCTs comprising 543 participants were included. Compared with pharmacotherapy alone, BEA as a monotherapy or adjunctive therapy to pharmacotherapy showed significant results at 5 min to 1 h after intervention in lowering systolic blood pressure, but not for diastolic blood pressure. BEA as a monotherapy showed no favorable long-term antihypertensive effects compared with pharmacotherapy. However, the long-term antihypertensive effect of combination therapy was better than the pharmacotherapy alone. Only one study reported adverse events and these were not serious. The methodological quality of included studies was generally low.

**Conclusion:** BEA as monotherapy or adjuvant therapy might have benefits in treating primary hypertension. Therefore, this treatment has the potential of non-pharmacological methods that can be used in patients attempting to withdraw antihypertensives or not responding to the conventional pharmacotherapy. However, since the number of studies included and the sample sizes were small, and the methodological quality was poor, these findings should be interpreted with great caution. Further well-designed studies need to be conducted to confirm these results.


Abstract:

Background: The Janus kinase 1 (JAK1) pathway has been implicated in the pathogenesis of psoriatic arthritis. We aimed to investigate the efficacy and safety of filgotinib, a selective JAK1 inhibitor, for the treatment of psoriatic arthritis.

Methods: The EQUATOR trial was a randomised, double-blind, placebo-controlled phase 2 trial that enrolled adults from 25 sites in seven countries (Belgium, Bulgaria, Czech Republic, Estonia, Poland, Spain, and Ukraine). Patients (aged ≥18 years) had active moderate-to-severe psoriatic arthritis (defined as at least five swollen joints and at least five tender joints) fulfilling Classification for psoriatic arthritis (CASPAR) criteria, active or a documented history of plaque psoriasis, and an insufficient response or intolerance to at least one conventional synthetic disease-modifying anti-rheumatic drug (csDMARD). Patients continued to take csDMARDs during the study if they had received this treatment for at least 12 weeks before screening and were on a stable dose for at least 4 weeks before baseline. Using an interactive web-based system, we randomly allocated patients (1:1) to filgotinib 200 mg or placebo orally once daily for 16 weeks (stratified by current use of csDMARDs and previous use of anti-tumour necrosis factor). Patients, study team, and sponsor were masked to treatment assignment. The primary endpoint was proportion of patients achieving 20% improvement in American College of Rheumatology response criteria (ACR20) at week 16 in the full analysis set (patients who received at least one dose of study drug), which was compared between groups with the Cochran-Mantel-Haenszel test and non-responder imputation method. This trial is registered with ClinicalTrials.gov, number NCT03101670.

Findings: Between March 9, and Sept 27, 2017, 191 patients were screened and 131 were randomly allocated to treatment (65 to filgotinib and 66 to placebo). 60 (92%) patients in the filgotinib group and 64 (97%) patients in the placebo group completed the study; five patients (8%) in the filgotinib group and two patients (3%) in the placebo group discontinued treatment. 52 (80%) of 65 patients in the filgotinib group and 22 (33%) of 66 in the placebo group achieved ACR20 at week 16 (treatment difference 47% [95% CI 30·2–59·6], p<0·0001). 37 (57%) patients who received filgotinib and 39 (59%) patients who received placebo had at least one treatment-emergent adverse event. Six participants had an event that was grade 3 or worse. The most common events were nasopharyngitis and headache, occurring at similar proportions in each group. One serious treatment-emergent adverse event was reported in each group (pneumonia and hip fracture after a fall), one of which (pneumonia) was fatal in the filgotinib group.
**Interpretation:** Filgotinib is efficacious for the treatment of active psoriatic arthritis, and no new safety signals were identified.

**Funding:** Galapagos and Gilead Sciences.


**Abstract:**

**Background:** 2.6 million pregnancies were estimated to have ended in stillbirth in 2015. The aim of the AFFIRM study was to test the hypothesis that introduction of a reduced fetal movement (RFM), care package for pregnant women and clinicians that increased women's awareness of the need for prompt reporting of RFM and that standardised management, including timely delivery, would alter the incidence of stillbirth.

**Methods:** This stepped wedge, cluster-randomised trial was done in the UK and Ireland. Participating maternity hospitals were grouped and randomised, using a computer-generated allocation scheme, to one of nine intervention implementation dates (at 3 month intervals). This date was concealed from clusters and the trial team until 3 months before the implementation date. Each participating hospital had three observation periods: a control period from Jan 1, 2014, until randomised date of intervention initiation; a washout period from the implementation date and for 2 months; and the intervention period from the end of the washout period until Dec 31, 2016. Treatment allocation was not concealed from participating women and caregivers. Data were derived from observational maternity data. The primary outcome was incidence of stillbirth. The primary analysis was done according to the intention-to-treat principle, with births analysed according to whether they took place during the control or intervention periods, irrespective of whether the intervention had been implemented as planned. This study is registered with [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), number NCT01777022.

**Findings:** 37 hospitals were enrolled in the study. Four hospitals declined participation, and 33 hospitals were randomly assigned to an intervention implementation date. Between Jan 1, 2014, and Dec, 31, 2016, data were collected from 409 175 pregnancies (157 692 deliveries during the control period, 23 623 deliveries in the washout period, and 227 860 deliveries in the intervention period). The incidence of stillbirth was 4.40 per 1000 births during the control period and 4.06 per 1000 births in the intervention period.
(adjusted odds ratio [aOR] 0.90, 95% CI 0.75–1.07; p=0.23).

**Interpretation:** The RFM care package did not reduce the risk of stillbirths. The benefits of a policy that promotes awareness of RFM remains unproven.

**Funding:** Chief Scientist Office, Scottish Government (CZH/4/882), Tommy’s Centre for Maternal and Fetal Health, Sands.


**Abstract:**

**Background:** Based on previous findings, we hypothesised that radiotherapy to the prostate would improve overall survival in men with metastatic prostate cancer, and that the benefit would be greatest in patients with a low metastatic burden. We aimed to compare standard of care for metastatic prostate cancer, with and without radiotherapy.

**Methods:** We did a randomised controlled phase 3 trial at 117 hospitals in Switzerland and the UK. Eligible patients had newly diagnosed metastatic prostate cancer. We randomly allocated patients open-label in a 1:1 ratio to standard of care (control group) or standard of care and radiotherapy (radiotherapy group). Randomisation was stratified by hospital, age at randomisation, nodal involvement, WHO performance status, planned androgen deprivation therapy, planned docetaxel use (from December, 2015), and regular aspirin or non-steroidal anti-inflammatory drug use. Standard of care was lifelong androgen deprivation therapy, with up-front docetaxel permitted from December, 2015. Men allocated radiotherapy received either a daily (55 Gy in 20 fractions over 4 weeks) or weekly (36 Gy in six fractions over 6 weeks) schedule that was nominated before randomisation. The primary outcome was overall survival, measured as the number of deaths; this analysis had 90% power with a one-sided α of 2.5% for a hazard ratio (HR) of 0.75. Secondary outcomes were failure-free survival, progression-free survival, metastatic progression-free survival, prostate cancer-specific survival, and symptomatic local event-free survival. Analyses used Cox proportional hazards and flexible parametric models, adjusted for stratification factors. The primary outcome analysis was by intention to treat. Two prespecified subgroup analyses tested the effects of prostate
radiotherapy by baseline metastatic burden and radiotherapy schedule. This trial is registered with ClinicalTrials.gov, number NCT00268476.

**Findings:** Between Jan 22, 2013, and Sept 2, 2016, 2061 men underwent randomisation, 1029 were allocated the control and 1032 radiotherapy. Allocated groups were balanced, with a median age of 68 years (IQR 63–73) and median amount of prostate-specific antigen of 97 ng/mL (33–315). 367 (18%) patients received early docetaxel. 1082 (52%) participants nominated the daily radiotherapy schedule before randomisation and 979 (48%) the weekly schedule. 819 (40%) men had a low metastatic burden, 1120 (54%) had a high metastatic burden, and the metastatic burden was unknown for 122 (6%). Radiotherapy improved failure-free survival (HR 0·76, 95% CI 0·68–0·84; p<0·0001) but not overall survival (0·92, 0·80–1·06; p=0·266). Radiotherapy was well tolerated, with 48 (5%) adverse events (Radiation Therapy Oncology Group grade 3–4) reported during radiotherapy and 37 (4%) after radiotherapy. The proportion reporting at least one severe adverse event (Common Terminology Criteria for Adverse Events grade 3 or worse) was similar by treatment group in the safety population (398 [38%] with control and 380 [39%] with radiotherapy).

**Interpretation:** Radiotherapy to the prostate did not improve overall survival for unselected patients with newly diagnosed metastatic prostate cancer.

**Funding:** Cancer Research UK, UK Medical Research Council, Swiss Group for Clinical Cancer Research, Astellas, Clovis Oncology, Janssen, Novartis, Pfizer, and Sanofi-Aventis.


Reuter Uwe, Goadsby Peter J, Lanteri Minet Michel et al. Efficacy and tolerability of erenumab in patients with episodic migraine in whom two-to-four previous preventive treatments were unsuccessful: A randomised, double-blind, placebo-controlled, phase 3b study. *Lancet* 2018; 392(10161): 2280-87p.

**Abstract:**

**Background:** A substantial proportion of patients with migraine does not respond to, or cannot tolerate, oral preventive treatments. Erenumab is a novel CGRP-receptor antibody with preventive efficacy in migraine. We assessed its efficacy and tolerability in patients with episodic migraine in whom previous treatment with two-to-four migraine preventives had been unsuccessful.

**Methods:** LIBERTY was a 12-week, double-blind, placebo-controlled randomised study at 59 sites in 16 countries. Eligible patients were aged 18–65 years and had a history of episodic migraine with or without aura for at least 12 months, had migraine for an average of 4–14 days per month during the 3 months before screening, and had been treated unsuccessfully (in terms of either efficacy or tolerability, or both) with between two and four
preventive treatments. Eligible participants were randomly assigned (1:1) to receive either erenumab 140 mg (via two 70 mg injections) or placebo every 4 weeks subcutaneously for 12 weeks. Randomisation was by interactive response technology and was stratified by monthly frequency of migraine headache (4–7 vs 8–14 migraine days per month) during the baseline phase. Cenduit generated the randomisation list and assigned participants to groups. Participants, investigators, people doing various assessments, and the study sponsor were masked to treatment assignment. The primary endpoint was the proportion of patients achieving a 50% or greater reduction in the mean number of monthly migraine days during weeks 9–12. Efficacy was measured in the full analysis set, which included all randomly assigned patients who started their assigned treatment and completed at least one post-baseline monthly migraine day measurement. Safety and tolerability were assessed by recording adverse events and by physical examination, assessment of vital signs, clinical laboratory assessments, and electrocardiography. Safety was assessed in all randomly assigned patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT03096834. The trial is closed to new participants, but the open-label extension phase is ongoing.

Findings: Between March 20, 2017, and Oct 27, 2017, 246 participants were randomly assigned, 121 to the erenumab group and 125 to the placebo group. 95 of 246 (39%) participants had previously unsuccessfully tried two preventive drugs, 93 (38%) had tried three, and 56 (23%) had tried four. At week 12, 36 (30%) patients in the erenumab had a 50% or greater reduction from baseline in the mean number of monthly migraine days, compared with 17 (14%) in the placebo group (odds ratio 2·7 [95% CI 1·4–5·2]; p=0·002). The tolerability and safety profiles of erenumab and placebo were similar. The most frequent treatment-emergent adverse event was injection site pain, which occurred in seven (6%) participants in both groups.

Interpretation: Compared with placebo, erenumab was efficacious in patients with episodic migraine who previously did not respond to or tolerate between two and four previous migraine preventive treatments. Erenumab might be an option for patients with difficult-to-treat migraine who have high unmet needs and few treatment options.

Funding: Novartis Pharma.


Smith Lucy K, Hindori Mohangoo Ashna D, Delnord Marie et al. Quantifying the burden of stillbirths before 28 weeks of completed

**Abstract:**

**Background:** International comparisons of stillbirth allow assessment of variations in clinical practice to reduce mortality. Currently, such comparisons include only stillbirths from 28 or more completed weeks of gestational age, which underestimates the true burden of stillbirth. With increased registration of early stillbirths in high-income countries, we assessed the reliability of including stillbirths before 28 completed weeks in such comparisons.

**Methods:** In this population-based study, we used national cohort data from 19 European countries participating in the Euro-Peristat project on livebirths and stillbirths from 22 completed weeks of gestation in 2004, 2010, and 2015. We excluded countries without national data for stillbirths by gestational age in these periods, or where data available were not comparable between 2004 and 2015. We also excluded those countries with fewer than 10,000 births per year because the proportion of stillbirths at 22 weeks to less than 28 weeks of gestation is small. We calculated pooled stillbirth rates using a random-effects model and changes in rates between 2004 and 2015 using risk ratios (RR) by gestational age and country.

**Findings:** Stillbirths at 22 weeks to less than 28 weeks of gestation accounted for 32% of all stillbirths in 2015. The pooled stillbirth rate at 24 weeks to less than 28 weeks declined from 0.97 to 0.70 per 1000 births from 2004 to 2015, a reduction of 25% (RR 0.75, 95% CI 0.65–0.85). The pooled stillbirth rate at 22 weeks to less than 24 weeks of gestation in 2015 was 0.53 per 1000 births and did not significantly changed over time (RR 0.97, 95% CI 0.80–1.16) although changes varied widely between countries (RRs 0.62–2.09). Wide variation in the percentage of all births occurring at 22 weeks to less than 24 weeks of gestation suggest international differences in ascertainment.

**Interpretation:** Present definitions used for international comparisons exclude a third of stillbirths. International consistency of reporting stillbirths at 24 weeks to less than 28 weeks suggests these deaths should be included in routinely reported comparisons. This addition would have a major impact, acknowledging the burden of perinatal death to families, and making international assessments more informative for clinical practice and policy. Ascertainment of fetal deaths at 22 weeks to less than 24 weeks should be stabilised so that all stillbirths from 22 completed weeks of gestation onwards can be reliably compared.

**Funding:** EU Union under the framework of the Health Programme and the Bridge Health Project.

Abstract:

Background: Previous studies have reported national and regional Global Burden of Disease (GBD) estimates for the UK. Because of substantial variation in health within the UK, action to improve it requires comparable estimates of disease burden and risks at country and local levels. The slowdown in the rate of improvement in life expectancy requires further investigation. We use GBD 2016 data on mortality, causes of death, and disability to analyse the burden of disease in the countries of the UK and within local authorities in England by deprivation quintile.

Methods: We extracted data from the GBD 2016 to estimate years of life lost (YLLs), years lived with disability (YLDs), disability-adjusted life-years (DALYs), and attributable risks from 1990 to 2016 for England, Scotland, Wales, Northern Ireland, the UK, and 150 English Upper-Tier Local Authorities. We estimated the burden of disease by cause of death, condition, year, and sex. We analysed the association between burden of disease and socioeconomic deprivation using the Index of Multiple Deprivation. We present results for all 264 GBD causes of death combined and the leading 20 specific causes, and all 84 GBD risks or risk clusters combined and 17 specific risks or risk clusters.

Findings: The leading causes of age-adjusted YLLs in all UK countries in 2016 were ischaemic heart disease, lung cancers, cerebrovascular disease, and chronic obstructive pulmonary disease. Age-standardised rates of YLLs for all causes varied by two times between local areas in England according to levels of socioeconomic deprivation (from 14 274 per 100 000 population [95% uncertainty interval 12 791–15 875] in Blackpool to 6888 [6145–7739] in Wokingham). Some Upper-Tier Local Authorities, particularly those in London, did better than expected for their level of deprivation. Allowing for differences in age structure, more deprived Upper-Tier Local Authorities had higher attributable YLLs for most major risk factors in the GBD. The population attributable fractions for all-cause YLLs for individual major risk factors varied across Upper-Tier Local Authorities. Life expectancy and YLLs have improved more slowly since 2010 in all UK countries compared with 1990–2010. In nine of 150 Upper-Tier Local Authorities, YLLs increased after 2010. For attributable YLLs, the rate of improvement slowed most substantially for cardiovascular disease and breast, colorectal, and lung cancers, and showed little change for Alzheimer’s disease and other dementias. Morbidity makes an increasing contribution to overall burden in the UK compared with mortality. The age-standardised UK DALY rate for low back and neck pain (1795 [1258–2356]) was higher than for ischaemic heart disease (1200 [1155–1246]) or lung cancer (660 [642–679]). The leading causes of ill health (measured through YLDs) in the UK in 2016 were low
back and neck pain, skin and subcutaneous diseases, migraine, depressive disorders, and sense organ disease. Age-standardised YLD rates varied much less than equivalent YLL rates across the UK, which reflects the relative scarcity of local data on causes of ill health.

**Interpretation:** These estimates at local, regional, and national level will allow policy makers to match resources and priorities to levels of burden and risk factors. Improvement in YLLs and life expectancy slowed notably after 2010, particularly in cardiovascular disease and cancer, and targeted actions are needed if the rate of improvement is to recover. A targeted policy response is also required to address the increasing proportion of burden due to morbidity, such as musculoskeletal problems and depression. Improving the quality and completeness of available data on these causes is an essential component of this response.

**Funding:** Bill & Melinda Gates Foundation and Public Health England.


**Abstract:**

**Background:** Preterm delivery during pregnancy (<37 weeks' gestation) is a leading cause of perinatal mortality and morbidity. Treating bacterial vaginosis during pregnancy can reduce poor outcomes, such as preterm birth. We aimed to investigate whether treatment of bacterial vaginosis decreases late miscarriages or spontaneous very preterm birth.

**Methods:** PREMEVA was a double-blind randomised controlled trial done in 40 French centres. Women aged 18 years or older with bacterial vaginosis and low-risk pregnancy were eligible for inclusion and were randomly assigned (2:1) to three parallel groups: single-course or triple-course 300 mg clindamycin twice-daily for 4 days, or placebo. Women with high-risk pregnancy outcomes were eligible for inclusion in a high-risk subtrial and were randomly assigned (1:1) to either single-course or triple-course clindamycin. The primary outcome was a composite of late miscarriage (16–21 weeks) or spontaneous very preterm birth (22–32 weeks), which we assessed in all patients with delivery data (modified intention to treat). Adverse events were systematically reported. This study is registered with ClinicalTrials.gov, number NCT00642980.

**Findings:** Between April 1, 2006, and June 30, 2011, we screened 84 530 pregnant women before 14 weeks' gestation. 5630 had bacterial vaginosis, of whom 3105 were randomly assigned to groups in the low-risk trial (n=943 to receive single-course clindamycin, n=968 to receive triple-course clindamycin, and n=958 to receive placebo) or high-risk subtrial (n=122 to receive single-course clindamycin and n=114 to receive triple-course clindamycin). In 2869 low-risk pregnancies, the primary outcome occurred in 22 (1·2%) of 1904 participants receiving clindamycin and 10 (1·0%) of 956
participants receiving placebo (relative risk [RR] 1·10, 95% CI 0·53–2·32; \(p=0·82\)). In 236 high-risk pregnancies, the primary outcome occurred in 5 (4·4%) participants in the triple-course clindamycin group and 8 (6·0%) participants in the single-course clindamycin group (RR 0·67, 95% CI 0·23–2·00; \(p=0·47\)). In the low-risk trial, adverse events were more common in the clindamycin groups than in the placebo group (58 [3·0%] of 1904 vs 12 [1·3%] of 956; \(p=0·0035\)). The most commonly reported adverse event was diarrhoea (30 [1·6%] in the clindamycin groups vs 4 [0·4%] in the placebo group; \(p=0·0071\)); abdominal pain was also observed in the clindamycin groups (9 [0·6%] participants) versus none in the placebo group (\(p=0·034\)). No severe adverse event was reported in any group. Adverse fetal and neonatal outcomes did not differ significantly between groups in the high-risk subtrial.

**Interpretation:** Systematic screening and subsequent treatment for bacterial vaginosis in women with low-risk pregnancies shows no evidence of risk reduction of late miscarriage or spontaneous very preterm birth. Use of antibiotics to prevent preterm delivery in this patient population should be reconsidered.

**Funding:** French Ministry of Health.


**Abstract:**

Implementation research is important in global health because it addresses the challenges of the know–do gap in real-world settings and the practicalities of achieving national and global health goals. Implementation research is an integrated concept that links research and practice to accelerate the development and delivery of public health approaches. Implementation research involves the creation and application of knowledge to improve the implementation of health policies, programmes, and practices. This type of research uses multiple disciplines and methods and emphasises partnerships between community members, implementers, researchers, and policy makers. Implementation research focuses on practical approaches to improve implementation and to enhance equity, efficiency, scale-up, and sustainability, and ultimately to improve people’s health. There is growing interest in the principles of implementation research and a range of perspectives on its purposes and appropriate methods. However, limited efforts have been made to systematically document and review learning from the practice of implementation research across different countries and technical areas. Drawing on an expert review process, this Health Policy paper presents purposively selected case studies to illustrate the essential characteristics of implementation research and its application in low-income and middle-income countries. The case studies are organised into four categories related to the purposes of using implementation research, including improving people’s health, informing policy design and implementation, strengthening health service delivery, and empowering...
communities and beneficiaries. Each of the case studies addresses implementation problems, involves partnerships to co-create solutions, uses tacit knowledge and research, and is based on a shared commitment towards improving health outcomes. The case studies reveal the complex adaptive nature of health systems, emphasise the importance of understanding context, and highlight the role of multidisciplinary, rigorous, and adaptive processes that allow for course correction to ensure interventions have an impact. This Health Policy paper is part of a call to action to increase the use of implementation research in global health, build the field of implementation research inclusive of research utilisation efforts, and accelerate efforts to bridge the gap between research, policy, and practice to improve health outcomes.


Abstract:

This report presents further evidence on the escalating alcohol consumption in the UK and the burden of liver disease associated with this major risk factor, as well as the effects on hospital and primary care. We reiterate the need for fiscal regulation by the UK Government if overall alcohol consumption is to be reduced sufficiently to improve health outcomes. We also draw attention to the effects of drastic cuts in public services for alcohol treatment, the repeated failures of voluntary agreements with the drinks industry, and the influence of the industry through its lobbying activities. We continue to press for reintroduction of the alcohol duty escalator, which was highly effective during the 5 years it was in place, and the introduction of minimum unit pricing in England, targeted at the heaviest drinkers. Results from the introduction of minimum unit pricing in Scotland, with results from Wales to follow, are likely to seriously expose the weakness of England’s position. The increasing prevalence of obesity-related liver disease, the rising number of people diagnosed with type 2 diabetes and its complications, and increasing number of cases of end-stage liver disease and primary liver cancers from non-alcoholic fatty liver disease make apparent the need for an obesity strategy for adults. We also discuss the important effects of obesity and alcohol on disease progression, and the increased risk of the ten most common cancers (including breast and colon cancers). A new in-depth analysis of the UK National Health Service (NHS) and total societal costs shows the extraordinarily large expenditures that could be saved or redeployed elsewhere in the NHS. Excellent results have been reported for new antiviral drugs for hepatitis C virus infection, making elimination of chronic infection a real possibility ahead of the WHO 2030 target. However, the extent of unidentified cases remains a problem, and will also apply when new curative drugs for hepatitis B virus become available. We also describe efforts to improve standards of hospital care for liver disease with better understanding of current service deficiencies and a new accreditation process.
for hospitals providing liver services. New commissioning arrangements for primary and community care represent progress, in terms of effective screening of high-risk subjects and the early detection of liver disease.


Abstract:

Introduction: Appraising quality of evidence (QoE) is an essential process for performing systematic reviews. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) is one of the tools for assessing QoE, however, concerns about its reliability and comprehensiveness have been raised. To address these shortcomings, we developed the Clinical and Health Intervention Meta-analysis Evidence Rating System (CHIMERAS).

Methods: A single-center, parallel randomized controlled trial was conducted to assess and compare the reliability of CHIMERAS and GRADE. Raters were randomly assigned into two groups. They were trained to use either GRADE or CHIMERAS for assessing QoE. QoE from 100 Cochrane systematic reviews (SRs) was assessed with GRADE in group 1 and CHIMERAS in group 2. Inter-rater reliability and inter-consensus reliability were evaluated by calculating the intra-class correlation (ICC).

Results: CHIMERAS showed moderate agreement (ICC = 0.54, 95% confidence interval [CI]: 0.44-0.64), while GRADE had fair agreement (ICC = 0.38, 95% CI: 0.28-0.49) for inter-rater reliability among individual raters. CHIMERAS showed substantial agreement (ICC = 0.78, 95% CI: 0.69-0.84), while GRADE had moderate agreement (ICC = 0.52, 95% CI: 0.36-0.65) for inter-consensus reliability across pairs of raters. With GRADE, respectively 77.0% and 11.0% SRs were judged as having low or very low, and high QoE. With CHIMERAS, respectively 10.0% and 54.0% SRs were judged as having low or very low, and high or very high QoE.

Conclusion: CHIMERAS outperformed GRADE in terms of inter-rater reliability and inter-consensus reliability. CHIMERAS and GRADE also showed substantial disagreement in grading QoE, indicating the possible impact on decision making attributable to varying rating approaches.

Trial registration: Protocol of this trial has been registered prospectively in the Chinese Clinical Trial Registry (Registration number: ChiCTR-IOR-16008898) on 13 July 2016.