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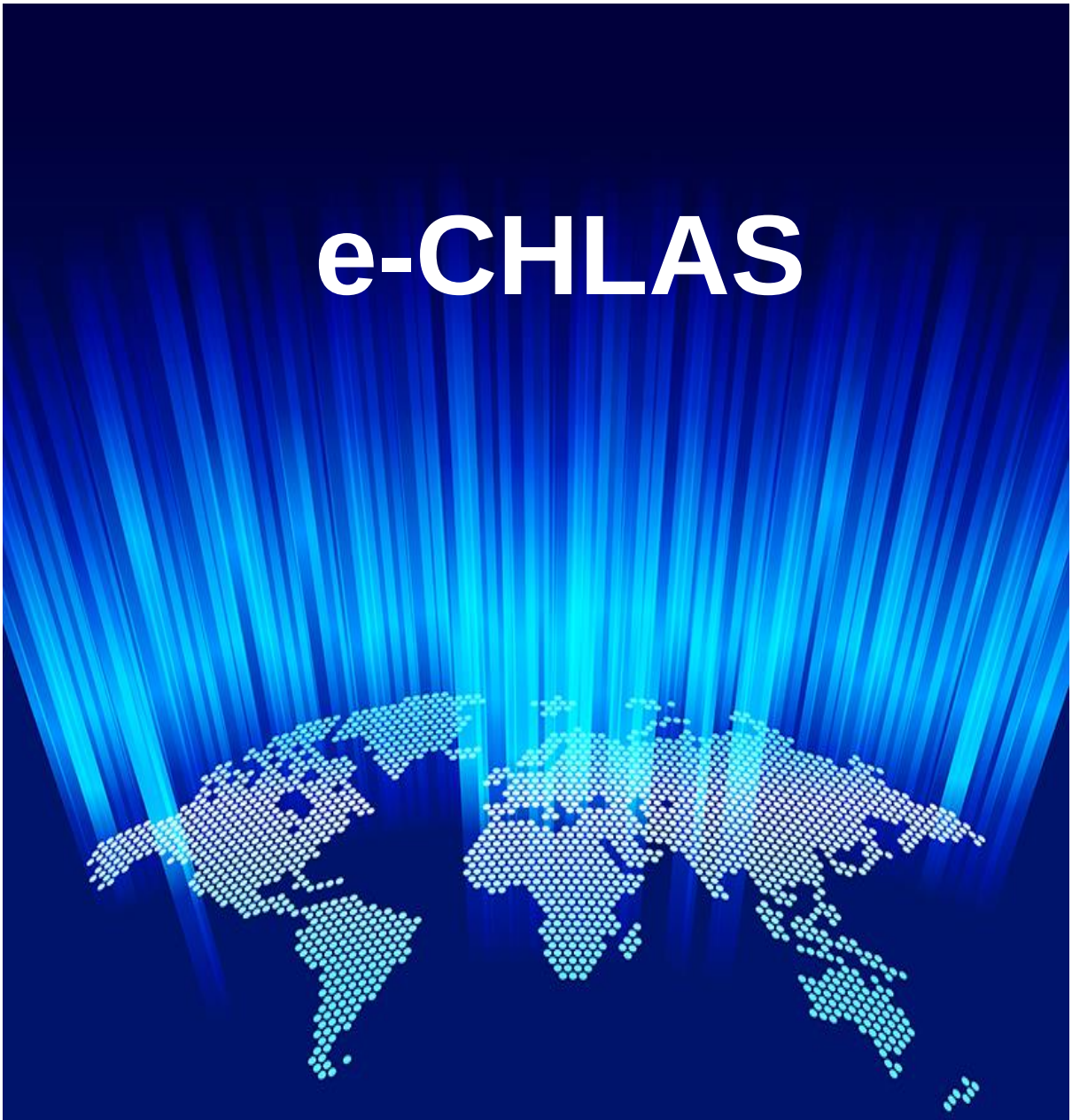

FEBRUARY 2022

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PREFACE

Introduction

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

Scope

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

Arrangement of Entries

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

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

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Acknowledgement

We are grateful to Dr. Subhash Kaushik, Director General, CCRH for his encouragement and valuable suggestions from time to time. We sincere acknowledge the cooperation of Mrs. Nisha Adhikari, Office Assistant in compiling this bulletin.

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AYUSH & Other System

Abdurahman Fatma, Payne Nicola. Reiki practitioners' perceptions of the impact of the COVID-19 pandemic on the experience, practice and future of Reiki. *Complementary Therapies in Clinical Practice 2022;*46: Article 101530

Abstract:

Objectives: This study examined the impact of the COVID-19 pandemic on the experience, practice and future of Reiki in the UK, including the personal impact of the pandemic on practitioners and their work, practitioner perceptions of the future of the profession and Reiki delivery, and practitioner experiences and views of distant Reiki in comparison to hands on or near the body treatments.

Method: A qualitative study using semi-structured interviews was carried out with 10 Reiki practitioners. Interviews were recorded, transcribed verbatim and analysed using thematic analysis.

Results: Three themes were identified: adapting and growing with the challenges of COVID-19, Reiki for individual and community resilience, and moving from the mainstream hands on to lesser known distant Reiki.

Conclusion: While the COVID-19 pandemic personally impacted Reiki practitioners, they focused on turning adversity into opportunity, to overcome a sense of disconnectedness and social isolation, by providing social support and promoting individual and community resilience. Practitioners focused on self-care, personal development and reaching out to the community. Personal Protective Equipment was perceived as necessary for infection control but a potential barrier to the client's experience of Reiki. They saw value in adapting their practice as part of the future of the profession by utilising new technology and distant Reiki healing, but were clear this could not replace in person contact.

Adel Mehraban Mohammad Sadegh, Tansaz Mojgan, Mohammadi Mohammad, Yavari Maryam. Effects of pomegranate supplement on menopausal symptoms and quality of life in menopausal women: A double-blind randomized placebo-controlled trial. *Complementary Therapies in Clinical Practice 2022;*46: Article 101544

Abstract:

Background: Menopausal symptoms have negative effects on the aspects of quality of life and impose a high cost on the health system. In traditional Persian medicine, pomegranate is recommended to alleviate menopausal symptoms.

Material and methods: A randomized double-blind placebo-controlled trial was performed among 78 healthy women. Participants were interviewed three times: Before receiving the supplement/placebo, after completing the treatment, and after 3 weeks with no intervention. They filled out the demographic information sheet, modified-Kupperman index, and Menopause-Specific Quality of Life (MENQOL) questionnaires.

Results: The mean scores of the modified-Kupperman index and MENQOL characteristics before and after the treatment and after the follow-up period were significantly different between pomegranate and placebo groups in both modified-Kupperman and MENQOL scores ($p < 0.001$).

Conclusion: This study demonstrated that 4 weeks' treatment with the pomegranate supplement significantly ameliorates the irritating symptoms of menopause and improves the quality of life in menopausal women even after 4 weeks' medicine deprivation.

Allan Norman. Explanation of Ultradilution and Potentization in Homeopathy. *Homeopathy 2022;* 111(1): 74-76p.

Abstract:

This thesis attempts to explain the phenomena of ultradilution and homeopathic potentization with an anecdotal account of a biotinylated dot-blot demonstration of ultradilution brought to the attention of the Pomeranz laboratory, University of Toronto, in 1989. It is argued that the dot-blots are not only data but that they are also an expression of ultradilution itself. Moreover, it is considered that ultradilution and homeopathic potentization can be explained by: (1) Poincaré's recurrence (the disappearance and return of the signal); (2) succussion, resonance and amplification (preservation of the signal); (3) quantum coherence domains (the nature of the signals); and (4) generation of harmonics (the transformation of the signal).

Amorim Diogo, Brito Irma, Caseiro Armando, Figueiredo Joao Paulo, Machado Jorge. Electroacupuncture and acupuncture in the treatment of anxiety: A double blinded randomized parallel clinical trial. *Complementary Therapies in Clinical Practice 2022;*46: Article 101541

Abstract:

Background: The estimated number of people living with anxiety disorders worldwide is around 264 million and is estimated to have worsened with the recent pandemic of COVID-19. Acupuncture has shown to have excellent therapeutic effects in reducing anxiety.

Design: Double-blinded randomized controlled clinical trial with 56 participants (21–82 years) with anxiety diagnosed by 3 different anxiety scales (BAI, GAD-7 and OASIS). A 30-min acupuncture session was applied once a week for 10 weeks.

Aims: Evaluate the effectiveness of acupuncture and electroacupuncture in the treatment of anxiety to verify if: (1) People with high anxiety report reduced scores after 5 and 10 sessions; (2) Salivary cortisol levels accompanied the reduced scores; (3) Electroacupuncture treatment is more effective than acupuncture; (4) the treatments is independent of anxiolytic medication.

Methods: Volunteers were randomized into 3 groups (control, acupuncture, and electroacupuncture). The results were analyzed by anxiety scales and salivary cortisol tests.

Results: The findings show an improvement in anxiety, assessed by BAI, GAD-7 and OASIS, after the 5th session of acupuncture ($p < 0.05$) and electroacupuncture ($p < 0.05$) and the 10th session for both techniques ($p < 0.001$). The salivary cortisol values measured in the morning followed this pattern ($p < 0.05$), although the reduction of the night cortisol values was not statistically significant. Electroacupuncture and acupuncture show similar efficacy. The positive effect after the treatments is independent of anxiolytic medication ($p < 0.001$).

Conclusion: Acupuncture and electroacupuncture are effective in treating anxiety on their own or as adjuncts to pharmacological therapy.

Anestin Annelie Sarah, Dupuis Gilles, Lanctot Dominique. Effects of the Bali Yoga Program for Breast Cancer Patients on Cancer Related Fatigue: Results of a Randomized Partially Blinded Controlled Trial. *Integrative and Complementary Therapies 2022;*28(1): 31-38p.

Abstract:

Background: A few complementary and alternative medicine methods have been reported to reduce cancer related fatigue (CRF). The purpose of this study was to evaluate the effects of a yoga intervention in reducing CRF among women receiving chemotherapy.

Materials and Methods: This was a randomized partially blinded controlled trial comparing a standardized yoga intervention to standard care. It was conducted at three medical centers in Montreal, Canada. Eligible patients were women diagnosed with stage I–III breast cancer receiving chemotherapy. Participants were randomly assigned to receive the yoga intervention immediately or after a waiting period. The Bali Yoga Program for Breast Cancer patients (BYP-BC) consisted of 24 gentle poses, 2 breathing techniques, relaxation periods, and psychoeducational themes. Participants attended eight weekly sessions lasting 90 minutes and a DVD

for home practice with 20- and 40-minute sessions. Participants in the waitlist (WL) control group received standard care.

Results: Forty-eight participants were included in the study. The repeated measure analyses revealed no significant increase in general fatigue in the BYP-BC group (P = 0.66) while it significantly worsened in the WL group (P = 0.000). Motivation improved in the BYP-BC group (P = 0.01) and worsened in the WL group (P = 0.01).

Conclusions: These preliminary results suggest BYP-BC could be beneficial in preventing worsening of CRF during chemotherapy.

Arcanjo Fabio Luciano, Martins Jose Vicente Pereira, Paulo Mote, Leporace Gustavo, Mansueto Gomes Neto. Proprioceptive neuromuscular facilitation training reduces pain and disability in individuals with chronic low back pain: A systematic review and meta-analysis. *Complementary Therapies in Clinical Practice 2022;*46: Article 101505

Abstract:

Background and purpose: Although proprioceptive neuromuscular facilitation (PNF) exercises are used in rehabilitation practice, their effects in patients with low back pain (LBP) remain unclear. This study aimed to investigate the efficacy of PNF training for pain and disability in patients with LBP.

Methods: In this systematic review, we searched five databases from the earliest date available to October 2020. Three comparisons were performed: PNF versus control, PNF versus core strengthening, and PNF versus conventional physical therapy.

Results: Sixteen studies met the eligibility criteria (722 patients). PNF training improved pain (standardized mean difference [SMD]: −2.6; 95% confidence interval [CI]: −4.2 to −0.9, n = 174) and disability (SMD: −3.29; 95% CI: −5.3 to −1.3, n = 144) compared to the control. PNF training also yielded a greater benefit for pain reduction (mean difference [MD]: −1.8, 95% CI: −2.2 to −0.3, n = 177) and disability improvement (MD: −6.6, 95% CI: −9.3 to −3.8, n = 113) than did core strengthening.

Conclusion: PNF training seems to be a useful strategy for decreasing pain and improving disability in patients with LBP. However, the quality of evidence for the outcomes of both pain and disability was low to moderate.

Babazadeh Zavieh Seyedeh Saeideh, Ansari Noureddin Nakhostin, Ghotbi Nastaran, Naghdi Soofia, Haeri Seyed Mohammad Jafar. Effects of dry needling plus exercise therapy on post-stroke spasticity and motor function: A case report. *Complementary Therapies in Clinical Practice 2022;*46: Article 101520

Abstract:

Background and purpose: The use of dry needling (DN) with other treatments may be more beneficial in managing post-stroke spasticity. We report the effects of DN plus exercise therapy (ET) on wrist flexor spasticity.

Patient presentation: The patient was a 45-year-old man with an 8-year history of stroke. The outcome measures included the Modified Modified Ashworth Scale (MMAS), Hmax/Mmax ratio, H-reflex latency, Action Research Arm Test (ARAT), Fugl-Meyer Assessment (FMA), and range of motion (ROM) which were assessed before (T1), after (T2), and after 3-week follow-up (T3).

Conclusion: The MMAS was improved at T2 from "3" to "2". The Hmax/Mmax decreased from 0.77 to 0.53 at T3. The H-reflex latency increased from 15.4 ms to 18.5 ms at T3. The wrist active and passive ROM increased ~30° and ~20° at T2, respectively. A 4-session DN plus ET may improve spasticity and ROM. No meaningful improvement was observed in function.

Bahceli Pinar Zorba, Arslan Selda, Ilik Yeter. Effect of slow-stroke back massage on chemotherapy-related fatigue in women with breast cancer: An assessor blinded, parallel group, randomized control trial. ***Complementary Therapies in Clinical Practice 2022;*****46: Article 101518**

Abstract:

Objective: This randomized controlled parallel-group trial was conducted to investigate the effect of slow-stroke back massage (SSBM) on the level of fatigue in women with breast cancer undergoing chemotherapy.

Methods: Sixty-four women with breast cancer receiving chemotherapy were randomly assigned to SSBMG (n:32), who received SSBM, and CG (n:32), who received routine treatment only. Women with breast cancer in the intervention group received SSBM for a total of 20 min, 10 min before and after each chemotherapy infusion (2nd, 3rd, and 4th cycle). The Brief Fatigue Inventory (BFI) was completed before and after three cycles of chemotherapy (2nd, 3rd, and 4th) to assess the level of fatigue in women with breast cancer.

Results: After using SSBM, the BFI score was significantly lower in SSBMG than in CG (p 0.001) at all three-time points (1st, 2nd, and 3rd-time points). While the within-group change (Δ) in SSBMG differed significantly between time points ($p = 0.018$, $\eta 2 = 0.14$), in contrast, the within-group change (Δ) in CG was found not to differ between time points.

Conclusion: This study has shown that SSBM, one of the non-pharmacological methods, has a positive effect on the level of fatigue in women with breast cancer.

Başkaya Ebru, Satl Demir. Effect of treatment adherence training given to patients with bipolar disorder on treatment adherence, social functioning and quality of life: A pilot study. *Complementary Therapies in Clinical Practice 2022;* 46: Article 101504

Abstract:

Background and purpose: Treatment non-adherence is quite common among patients with bipolar disorder, negatively affects the social functioning of patients and reduces the quality of life. This pilot study aims to measure the effect of treatment adherence training given to patients with bipolar disorder on treatment adherence, social functioning and quality of life.

Materials and methods: The pilot study was conducted with 40 bipolar disorder patients, 19 in the intervention group and 21 in the control group, using a quasi-experimental research design. The data were collected using the Participant Information Form, Medication Adherence Rating Scale, Social Functioning Scale and Short Form of the World Health Organization Quality of Life Questionnaire. Treatment adherence training was given once a week individually for a total of five sessions.

Results: There was no significant difference between the demographic characteristics and pre-test scale scores of the patients in the intervention and control groups before the treatment adherence training ($p > 0.05$). The mean treatment adherence, social functioning and quality of life scores of the patients in the intervention group were higher in the post-test and follow-up test compared to the patients in the control group ($p < 0.001$).

Conclusion: The intervention had a positive effect on treatment adherence, social functioning and quality of life of patients. Considering the promising results of this pilot study, treatment adherence training should be studied further in the patients with biplor disorder.

Bennetts Alison. How does yoga practice and therapy yield psychological benefits? A review and model of transdiagnostic processes. *Complementary Therapies in Clinical Practice 2022;*46: Article 101514

Abstract:

Interest in yoga as an intervention for psychological wellbeing has increased in recent years, with literature investigating beneficial effects in a variety of presentations and settings. The theoretical understanding of this benefit has previously focused on physiological changes involved in yoga practice, however interest has turned to the potential psychological mechanisms eliciting psychological wellbeing.

The current paper builds on previous theory and argues that yoga practice targets transdiagnostic psychological processes; mechanisms that feature commonly across a wide range of presentations, thus reducing distress and increasing wellbeing across clinical and non-clinical populations. Features of yoga practice are discussed in relation to these transdiagnostic processes and the features of modern talking therapies. A new model is proposed positing specific aspects of yoga practice correlate with specific transdiagnostic processes to elicit psychological change and argues that the mechanisms by which change occurs are directly compared with the changes observed in talking therapies. The implications for future research and the potential for this to support the commissioning of holistic approaches in clinical practice are discussed.

Bordoni B, Walkowski S, Escher A, Ducoux B. Importance of the Posterolateral Area of the Diaphragm Muscle for Palpation and for the Treatment of Manual Osteopathic Medicine. *Complementary Medicine Research 2022;*29(1): 74-82p.

Abstract:

The eupneic act in healthy subjects involves a coordinated combination of functional anatomy and neurological activation. Neurologically, a central pattern generator, the components of which are distributed between the brainstem and the spinal cord, are hypothesized to drive the process and are modeled mathematically. A functionally anatomical approach is easier to understand although just as complex. Osteopathic manipulative treatment (OMT) is part of osteopathic medicine, which has many manual techniques to approach the human body, trying to improve the patient's homeostatic response. The principle on which OMT is based is the stimulation of self-healing processes, researching the intrinsic physiological mechanisms of the person, taking into consideration not only the physical aspect, but also the emotional one and the context in which the patient lives. This article reviews how the diaphragm muscle moves, with a brief discussion on anatomy and the respiratory neural network. The goal is to highlight the critical issues of OMT on the correct positioning of the hands on the posterolateral area of the diaphragm around the diaphragm, trying to respect the existing scientific anatomical-physiological data, and laying a solid foundation for improving the data obtainable from future research. The correctness of the position of the operator's hands in this area allows a more effective palpatory perception and, consequently, a probably more incisive result on the respiratory function.

Burnett Zeigler Inger, McLeod II Dennis. Diversifying Mindfulness: Reflections from Our Journeys Applying Mindfulness-Based Interventions in the Black Community. *Journal of Integrative and Complementary Medicine 2022;*28(2): 110-13p.

Cai Qian, Cai Shu bin, Chen Jian kun, Bai Xiao Hui, Li Ji Qiang. Tai Chi for anxiety and depression symptoms in cancer, stroke, heart failure, and chronic obstructive pulmonary disease: A systematic review and

meta-analysis. ***Complementary Therapies in Clinical Practice 2022;*****46: Article 101510**

Abstract:

Background: Many middle-aged and older adults have more than one chronic health condition. It is therefore important to explore the effectiveness of interventions for multiple chronic conditions. Tai Chi is widely used in China and other countries, and many studies have examined the effect of Tai Chi on anxiety and depression. However, there are no systematic reviews of the effect of Tai Chi on anxiety and depression in various chronic conditions. This systematic review and meta-analysis aimed to evaluate the effects of Tai Chi on anxiety and depression symptoms in four chronic conditions: cancer, stroke, heart failure (HF), and chronic obstructive pulmonary disease (COPD).

Methods: We searched Chinese and English databases (Cochrane Library, PubMed, Web of Science, China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (VIP), Wanfang Database, and Sinomed) from inception to October 2020. Review Manager version 5.2 and Stata version 12.0 were used to perform a systematic review. The quality of the included studies was evaluated using the Cochrane risk of bias tool. The study was registered with the PROSPERO database (number CRD42020209594).

Results: Of the 596 studies identified, we included 25 randomized controlled trials involving 1819 participants. Combined analysis of the four diseases showed statistically significant differences between the Tai Chi and control groups for anxiety symptoms (SMD −0.99, 95%CI: −1.5, −0.47; $P < 0.01$) and depressive symptoms (SMD 0.70, 95%CI: −1.01, −0.39; $P < 0.01$). Subgroup analyses showed statistically significant differences between the Tai Chi and control groups for depressive symptoms in stroke (SMD −0.43, 95%CI: −0.67, −0.18; $P < 0.01$) and HF (SMD −0.57, 95%CI: −0.8, −0.33; $P < 0.01$). However, no statistically significant differences were found for depressive symptoms in COPD or cancer. There were statistically significant differences between the Tai Chi and control groups for anxiety symptoms in stroke (SMD −0.60, 95%CI: −0.88, −0.32; $P < 0.01$) and cancer (SMD −0.69, 95%CI: −1.22, −0.17; $P < 0.01$), but not in COPD or HF. Subgroup, sensitivity, meta regression, and publication bias analyses showed high heterogeneity correlated with a single study and study quality. Sensitivity analysis showed that most meta-analysis results had good stability, but those for anxiety symptoms in COPD were unstable; therefore, careful interpretation is required.

Conclusion: Tai Chi has a positive effect on anxiety and depression, especially for patients with cancer, stroke, and HF. However, given the weak evidence, this approach is not a substitute for psychiatric treatment.

Carvalho Jozelio Freire de. Successful treatment of ankylosing spondylitis with alternative and complementary medicine withdrawal of adalimumab treatment. *Complementary Therapies in Clinical Practice 2022;* 46: Article 101494

Abstract:

Background and purpose: Current treatment strategies for ankylosing spondylitis (AS) include adalimumab and other biological drugs. However, treatment failures and side effects are commonly observed. This report documents the successful use of supplements and dietary changes to treat a patient with AS after cessation of adalimumab therapy.

Patient presentation: A 38-year-old human leukocyte antigen B27 positive female patient with AS showed no improvement when treated with a non-steroidal anti-inflammatory drug. The patient then began adalimumab therapy with some success; however, after nine months, she developed a disseminated and refractory Molluscum contagiosum infection. Adalimumab was withdrawn, and the patient started taking supplements, while adopting an anti-inflammatory diet (dairy-free, gluten-free, and sugar-free). Normalization of inflammatory markers was achieved after two months, and magnetic resonance imaging of the sacroiliac revealed a notable physical improvement.

Cramer Holger. Other Pandemic: Mental Health Before, During, and After COVID-19. *Journal of Integrative and Complementary Medicine 2022;*28(2): 108-09p.

Dai Yan Qi, Weng Heng, Wang Qing, Guo Xiu Jun, Huang Li. Moxibustion for diarrhea-predominant irritable bowel syndrome: A systematic review and meta-analysis of randomized controlled trials. *Complementary Therapies in Clinical Practice 2022;*46: Article 101532

Abstract:

Purpose: Diarrhea-predominant irritable bowel syndrome (IBS-D) is a common functional gastrointestinal disorder that imposes heavy burden on individuals and society. Asan external therapy of traditional Chinese medicine (TCM), moxibustion is usually used to treat IBS-D. This study aimed to explore the efficacy of moxibustion in treating patients with IBS-D.

Methods: A systematic search for randomized controlled trials (RCTs) that reported the use of moxibustion in IBS-D treatment was performed in eight databases.

Results: Eleven RCTs including 725 participants meet the inclusion criteria. Compared with other positive treatments (Western medicine, TCM prescription, and acupuncture), moxibustion treatment had superior effects against IBS-D according to the meta-analysis.

Conclusion: This systematic review provided preliminary research evidence that moxibustion is effective in treating IBS-D. Rigorously designed and large-scale RCTs are required to provide more robust evidence in this area.

Dey S, Shaikh AR, Saha S, Agrawal E, Gautam AK, Karuppusamy A et al. Efficacy of Individualized Homeopathic Medicines in the Treatment of Atopic Dermatitis in Adults: A Double-Blind, Randomized, Placebo-Controlled, Preliminary Trial. *Complementary Medicine Research 2022;*29(1): 17-26p.

Abstract:

Introduction: Individualized homeopathy (IH) in atopic dermatitis (AD) remained under-researched.

Objective: We aimed at evaluating efficacy of IH in AD.

Methods: A double-blind, randomized, placebo-controlled, short-term, preliminary trial was conducted in an Indian homeopathy hospital. Patients were randomized to either IH (n = 30) or identical-looking placebo (n = 30) using computerized randomization and allocation. Outcomes were patient-oriented scoring of AD (PO-SCORAD; primary end point), Dermatological Life Quality Index (DLQI) score, and AD burden score for adults (ADBSA; secondary end points), measured monthly for 3 months. An intention-to-treat sample was analyzed after adjusting baseline differences.

Results: On PO-SCORAD, improvement was higher in IH against placebo, but nonsignificant statistically ($p_{month\ 1} = 0.433$, $p_{month\ 2} = 0.442$, $p_{month\ 3} = 0.229$). Secondary outcomes were also nonsignificant – both DLQI and ADBSA ($p > 0.05$). Four adverse events (diarrhea, injury, common cold) were recorded.

Conclusions: There was a small, but nonsignificant direction of effect towards homeopathy, which renders the trial inconclusive. A properly powered robust trial is indicated.

Dilokthornsakul W, Rinta A, Dhippayom T, Dilokthornsakul P. Efficacy and Safety of Ginger regarding Human Milk Volume and Related Clinical Outcomes: A Systematic Review of Randomized Controlled Trials. *Complementary Medicine Research 2022;*29(1): 67-73p.

Abstract:

Background: Ginger has been used as a galactagogue in Southeast Asian countries. However, limited evidence of its effect has been reported. This

systematic review summarizes the efficacy and safety of ginger regarding human milk volume.

Methods: A systematic review was conducted. Randomized controlled trials (RCTs) which studied the effect of ginger on human milk volume were included. The primary outcome was 24-h human milk volume.

Results: We found five RCTs. Two studies reported ginger as a single intervention, while three studies reported ginger in a combination with other herbs. We found that ginger could enhance human milk volume in mothers with vaginal births. It failed to improve human milk volume in mothers with cesarian section (C-section). Ginger in several combination products has been shown to be effective in enhancing human milk volume, including ginger with pandan, with turmeric and fenugreek, and with Xiong-gui-tiao-xue-yin. No adverse effect directly related to ginger was reported.

Discussion: Ginger could be used to enhance human milk volume in mothers with vaginal births, but not in mothers with C-section. Combined ginger products could also be considered to improve human milk volume. These findings could guide healthcare providers or mothers to consider using ginger to increase human milk production.

Dutta Abhijit, Aruchunan Mooventhan, Mukherjee Anindya, Metri Kashinath G, Ghosh Kuntal, Basu Ray Indranill. Comprehensive Review of Yoga Research in 2020. *Journal of Integrative and Complementary Medicine 2022;*28(2): 114-23p.

Abstract:

Objectives: Accumulated evidence garnered in the last few decades has highlighted the role of yoga in health and disease. The overwhelming mortality and morbidity mediated by noncommunicable epidemics such as heart disease and cancer have fostered a search for mechanisms to attenuate them. Despite overwhelming success in acute care, the efficacy of modern medicines has been limited on this front. Yoga is one of the integrative therapies that has come to light as having a substantial role in preventing and mitigating such disorders. It thus seems trite to analyze and discuss the research advancements in yoga for 2020. The present review attempts to distill recent research highlights from voluminous literature generated in 2020.

Methods: This review was conducted on the articles published or assigned to an issue in 2020. The authors searched the PubMed database for clinical studies published in the English language, using yoga (including meditation) as the intervention, and having an adequate description of the intervention. Then, they extracted data from each study into a standardized Google sheet.

Results: A total of 1149 citations were retrieved in the initial search. Of these, 46 studies met eligibility criteria and were finally included. The

studies were predominantly on mental health and neuropsychology, addressing various issues such as anxiety, postural balance, migraine, academic performance, and childhood neglect. Anxiety, stress, and depression were other common denominators. Eight studies were on cardiorespiratory systems, including exercise capacity, cardiac rehabilitation, myocardial infarction, and hypertension. Three studies were on diabetes, evaluating the effect of yoga. Five studies focused on cognition, health status, and autonomic regulation and few others included cancers, infertility, ulcerative colitis, urinary incontinence, restless leg syndrome, rheumatoid arthritis, chronic pain, and metabolic syndrome. Finally, most studies were on noncommunicable diseases with one exception, human immunodeficiency virus; two randomized controlled trials were dedicated to it.

Conclusions: Yoga has been studied under a wide variety of clinicopathological conditions in the year 2020. This landscape review intends to provide an idea of the role of yoga in various clinical conditions and its future therapeutic implications.

Elpidoforou Michail, Bakalidou Daphne, Drakopoulou Maria, Kavga Anna, Stefanis Leonidas. Effects of a structured dance program in Parkinson's disease. A Greek pilot study. *Complementary Therapies in Clinical Practice 2022;*46: Article 101528

Abstract:

Introduction: Dance for Parkinson's Disease® (DfPD®) is a structured dance program that has never been evaluated in Greek PD population. This study assesses for the first time the efficacy, safety and feasibility of DfPD® program in Greek PD patients.

Material and methods: A total of 16 early-to-mid-stage PD patients (50% men, aged 56 ± 12) underwent a total of 16 60-min classes of adjusted to Greek music and dance culture DfPD®, twice weekly, over 8 weeks. Assessments were performed at baseline and at the end of the study period and included quality of life (PDQ-8), depressive symptoms (BDI-II), fatigue (PFS-16), cognitive functions (MoCA), balance (BBS) and body mass index (BMI). Safety (possible falls, injuries, muscle soreness or excessive fatigue) and feasibility (technical and financial parameters, willingness for participation and continuation, recruitment rates) were also assessed.

Results: Statistically significant improvements were found in quality of life (29 ± 47%, p = 0,020), depressive symptoms (26 ± 52%, p = 0,046), fatigue (13 ± 20%, p = 0,021), cognitive functions (17 ± 23%, p = 0,010), balance (5 ± 4%, p = 0,003) and BMI (2 ± 2%, p = 0,010). No adverse events, high adherence (93,75%) and low attrition (12,5%) rates were reported.

Conclusion: A twice weekly 60-min DfPD® class for 8 weeks is a safe and feasible non-pharmacological complementary therapeutic intervention for Greek PD patients and may improve their quality of life, depressive

symptoms, fatigue, cognitive functions, balance, and BMI. Further research on this intervention is warranted.

Fogarty Sarah, Hay Phillipa, Calleri Felicia, Fiddes Lisa, Barnett Rebecca, Baskwill Amanda. Impact of the COVID-19 Pandemic on the Professional Identity of Massage Therapists: The Reporting of a Quantitative Strand of a Mixed-Methods Study. *Journal of Integrative and Complementary Medicine 2022;*28(2): 124-35p.

Abstract:

Introduction: In late 2019, a pathogen outbreak occurred that rapidly spread, resulting in the coronavirus disease 2019 (COVID-19) global pandemic. Governments responded to the pandemic with a range of strategies, including forced quarantines and nationwide lockdowns. Research on professional identity during the pandemic has predominately focused on health care providers declared as "essential" rather than "nonessential." In this study, the authors examine the impacts on the professional identity of massage therapists (MTs) who were predominately deemed as nonessential health care providers during the COVID-19 pandemic.

Materials and methods: An online, questionnaire-based study sought to answer "In what ways has the professional identity of MTs in Canada and Australia been impacted by the COVID-19 global pandemic?" MTs in Canada and Australia were recruited using convenience sampling through e-mail and social media. A questionnaire was developed and pilot tested before implementation.

Results: Six hundred and forty-nine MTs participated (329 from Canada and 316 from Australia). Known constructs of professional identity that were affected during the pandemic included not feeling respected as a health care practitioner, feeling less professional than other health care providers, and experiencing burnout. New constructs that may have developed out of the pandemic and the measures established to manage them included being classified as nonessential and feeling a sense of camaraderie and belonging.

Conclusions: This study is the first of its kind to report the impact of the COVID-19 pandemic on the professional identity of MTs. The emerging constructs reported will be used to create interview questions for the subsequent qualitative strand of this explanatory mixed-methods study. In the qualitative study, respondents will be invited to share their experiences with their own voice to further the understanding of the impact of the COVID-19 pandemic on MTs' professional identity.

Fortun Rabadan Rocio, Sierra Artal Beatriz, Jimenez Sanchez Carolina. Effectiveness of intracavitary monopolar dielectric radiofrequency in women with endometriosis-associated pain: A case series. *Complementary Therapies in Clinical Practice 2022;*46: Article 101517

Abstract:

Background and Purpose: Endometriosis-associated pain is the main cause of chronic pelvic pain in women. Endometriosis has a significant negative impact across different domains of patients' quality of life. This study aimed to evaluate the efficacy of an intracavitary application of monopolar dielectric radiofrequency in women with endometriosis-associated pain.

Patient presentation: Five women with endometriosis received 25 sessions of an intracavitary application of monopolar dielectric radiofrequency within three months. Outcomes, including quality of life, sex interference (Endometriosis Health Profile [EHP]-30 + section C), myofascial pain syndrome (myofascial trigger points), pain intensity (Visual Analogue Scale), frequency and referral pattern, pressure pain thresholds, allodynia and neuropathic pain (modified DN4), were examined both during and outside menses, after intervention and six months later.

Results: Clinically meaningful improvements were achieved by most participants regarding pelvic pain intensity, abdominal sensitivity, and myofascial pain of the pelvic floor.

Conclusion: This study lays the foundation for future in-depth research, suggesting that monopolar dielectric radiofrequency could be helpful in improving the symptomatology and quality of life of women with endometriosis, also in patients who are unresponsive to medical and/or surgical treatments, or who cannot undergo them in the short term.

Goo Bonhyuk, Kim Jung Hyun, Kim Eun Jung, Lee Hyun Jong, Seo Byung-Kwan. Thread embedding acupuncture for herniated intervertebral disc of the lumbar spine: A multicenter, randomized, patient-assessor-blinded, controlled, parallel, clinical trial. *Complementary Therapies in Clinical Practice 2022;*46: Article 101538

Abstract:

Background and purpose: Although several studies have reported that thread embedding acupuncture (TEA) is effective for lumbar herniated intervertebral disc (LHIVD), the evidence remains limited because previous studies had a high risk of bias. This study aimed to investigate the efficacy and safety of TEA for LHIVD through a rigorously designed trial.

Materials and methods: This was a randomized, patient-assessor-blinded, sham-controlled trial. Participants were screened according to eligibility criteria, and 70 patients with LHIVD were randomly allocated to the TEA and sham TEA (STEA) groups in a 1:1 ratio. Both groups received TEA or STEA treatment at 23 acupoints once per week for eight weeks. Changes in low back pain, radiating pain, Oswestry disability index, Roland–Morris

disability questionnaire, EuroQol 5–Dimensions 5–Levels, and global perceived effect were measured at baseline and at 4, 8, 12, and 16 weeks after screening and compared between the two groups.

Results: TEA showed no significant difference in all outcomes compared to STEA immediately after eight weeks of treatment. After an additional eight weeks of follow-up, TEA showed a more significant effect on the low back pain than STEA ($p < 0.05$) and showed a better tendency in maintaining or enhancing the improvement of radiating pain, function, and quality of life even after the end of treatment. No serious adverse events were observed.

Conclusion: TEA is effective in improving low back pain in patients with LHIVD and may help improve function and quality of life, especially in the long term.

Harnett Joanna E, Rickwood Catherine, Steel Amie, Bradley Ryan. Naturopathic practitioners' approach to caring for people with cardiovascular disease risk factors: A cross-cultural cross-sectional study reporting the providers perspective. *Complementary Therapies in Clinical Practice 2022;*46: Article 101511

Abstract:

Background and purpose: Naturopathic practitioners (NPs) in the United States (US) and Australia are consulted for the prevention and management of a range of health conditions, including cardiovascular disease (CVD). Despite this, little is known about how NPs approach the management of CVD risk factors. The aim of this study was to explore NPs approach to the care of people with CVD risk factors.

Materials and methods: In 2018, Australian and US NPs were recruited via professional representative organisations. A survey was developed containing four domains; naturopathic approaches to the clinical management of CVD risk factors, communication and sharing of information; professional-client relationship factors; and demographic information. The data analysis was conducted using the appropriate statistical tests.

Results: A total of 151 NPs completed the survey (Australia n = 75, US n = 76). NPs reported employing dietary, and multiple behavioural and natural product interventions to treat CVD risk factors. The most frequently recommended products by US and Australian NPs were fish oils (87%), magnesium (83%) and coenzyme Q10 (87%). Differences in what US and Australian NPs recommended were identified. NPs reported limited communication with medical doctors about their clients. NPs placed high importance on the relationship quality with their clients.

Conclusion: US and Australian NPs represent an aspect of primary care and disease prevention that warrants further research that evaluates the potential risks and benefits of NP care, and challenges and opportunities

associated with NPs integration into the healthcare systems, for populations with CVD risk factors.

Hart Jane. Positive Psychology: One Way to Empower Patients During the Pandemic. *Integrative and Complementary Therapies 2022;*28(1): 28-30p.

Helha Fernandes Nascimento Maria, Wang Yuan Pang. Trends in complementary and alternative medicine for the treatment of common mental disorders: A bibliometric analysis of two decades. *Complementary Therapies in Clinical Practice 2022;*46: Article 101531

Abstract:

Objective: To investigate the trend of scientific production in relation to the modalities of CAM adopted for the treatment of common mental disorders (CMD), and the evolution and distribution of relevant articles.

Material and methods: A bibliometric analysis of studies published between 2001 and 2020 was performed, extracted from the Scopus database, using the terms: integrative medicine, complementary therapy, common mental disorders, anxiety and depression, and synonyms. The relationship between the number of publications, and the years studied were analyzed using Pearson's correlation, followed by linear regression to estimate the number of articles along with the year. The VOSviewer software was used to analyze scientometric data. The study looked at countries with the highest number of publications and citations, co-authorships, most frequent keywords, and leading research organizations.

Results: In the analysis of the two decades, we identified a high positive correlation between the number of publications and year (r = 0.945). In trend analysis, the linear regression equation predicted the growth of publications along with the year, with R2 = 0.8949 explaining most of the data variability. Spirituality was the most frequent term among the modalities. The concentration of publications and the number of citations were significantly higher in developed countries.

Conclusion: The rise in the number of publications in the past two decades on the application of CAM among individuals with CMD suggests a growing scientific interest in Integrative practices. These bibliometric indicators suggest that new studies are warranted, as well as improvements in public health policies.

Hoegmark Simon, Andersen Tonny Elmose, Grahn Patrik, Roessler Kirsten K. Wildman Programme: Experiences from a first implementation of a nature-based intervention designed for men with stress and chronic illnesses. *Complementary Therapies in Clinical Practice 2022;*46: Article 101535

Abstract:

Background and purpose: In Denmark attractive rehabilitation offers for men are lacking. Consequently, more men than women say no to participate in and more often drop out of rehabilitation programs. Therefore, a nature-based rehabilitation program called the 'Wildman Programme' has been designed to men. The 'Wildman Programme' combines nature experiences, body awareness training, mind relaxation, and supporting community spirit. The method is called Nature-Body-Mind-Community (NBMC). The aim of this study was to assess the implementability and effect of the 'Wildman Programme' on the participants' quality of life and symptoms of stress.

Materials and methods: The 'Wildman Programme' was explored as a quasi-experimental study. The study included 20 men with psychological stress and diminished quality of life due to mental health challenges and chronic illnesses. The primary outcome was quality of life and the secondary outcome was stress level. All outcomes were measured at baseline (T1) and at the end of the 'Wildman Programme' (T2).

Results: The study showed the 'Wildman Programme' has potential to reduce stress symptoms (15.40%) and enhance quality of life (10.07%) among the male participants. Furthermore, physical health (13.92%) and psychological health (16.88%) in relation to quality of life increased during the program.

Conclusion: The study showed that the 'Wildman Programme' is implementable in a Danish healthcare center. It was well received by the health professionals and the method was in demand by the target group of men. However, a larger study should be conducted to further investigate the findings of this study.

Hosomi JK, Facina AdS, Simoes MdJ, Nakamura MU. Effects of Bryophyllum pinnatum Administration on Wistar Rat Pregnancy: Biochemical and Histological Aspects. *Complementary Medicine Research 2022;*29(1): 35-42p.

Abstract:

Introduction: Bryophyllum pinnatum is widely used in folk medicine. It has neuropharmacological, anti-inflammatory, immunomodulatory, antidiabetic, hepatoprotective, and nephroprotective effects, among others. It also acts on uterine contractility. It is prescribed by practitioners of anthroposophic medicine for preterm labor, insomnia, and emotional disorders, and has other potential uses in obstetrics. As all drugs currently used in preterm labor have side effects, new tocolytic agents remain an area of active research.

Objective: To evaluate the effect of B. pinnatum mother tincture (MT) on albino rats and their offspring throughout pregnancy from a biochemical and histological standpoint.

Methods: Longitudinal, prospective, randomized controlled bioassay. This is the second stage of a trial that investigated 60 animals distributed across six equal groups: controls C1 and C2, which received 1 and 25 times the vehicle dose (30% ethanol), B1 and B2 (1- and 25-fold doses of B. pinnatum MT), and B3 and B4 (which received 50- and 100-fold doses of B. pinnatum concentrate). At this stage, blood chemistry parameters (glucose, alanine aminotransferase [ALT], aspartate aminotransferase [AST], creatinine, and blood urea nitrogen) were measured in dams, as well as histological aspects of dam liver, kidney, placenta, and uterine tissue and fetal liver, kidney, heart, and brain.

Results: No differences were found between group B1 (therapeutic dose) and its control C1 in relation to glucose, AST, ALT, and creatinine. Group B2 exhibited lower glucose levels than groups C1, B3, and B4. There was no difference in AST across groups. Groups B3 and B4 exhibited higher ALT levels than groups C1 and B1. Groups B1–B4 exhibited higher urea nitrogen levels than group C1. Creatinine levels were higher in groups B2 and B3 than group C1. On morphological evaluation, fatty infiltration of the liver was observed in the alcoholic vehicle control groups (C1 and C2).

Conclusions: Daily administration of B. pinnatum at therapeutic doses (group B1) to pregnant albino rats appears to be safe, with reduced glucose at dose B2, elevated ALT at doses B3 and B4, and increased urea at doses B1 to B4 and creatinine at B2 and B3, but never exceeding the normal reference range. It was not associated with histological changes in specimens of the maternal or fetal structures of interest.

Huang Alison J, Chesney Margaret A, Schembri Michael, Pawlowsky Sarah, Nicosia Francesca, Subak Leslee L. Rapid Conversion of a Group-Based Yoga Trial for Diverse Older Women to Home-Based Telehealth: Lessons Learned Using Zoom to Deliver Movement-Based Interventions. *Journal of Integrative and Complementary Medicine 2022;*28(2): 188-92p.

Abstract:

This brief report describes the rapid conversion of a randomized trial of a Hatha-based yoga program for older women with urinary incontinence to a telehealth videoconference platform during the coronavirus disease 2019 (COVID-19) pandemic. Interim results demonstrate the feasibility of recruiting and retaining participants across a wide range of ages and ethnic backgrounds, but also point to potential obstacles and safety concerns arising from telehealth-based instruction. The investigators present lessons learned about the benefits and challenges of using telehealth platforms to deliver movement-based interventions and consider strategies to promote

accessible and well-tolerated telehealth-based yoga programs for older and diverse populations.

Ito Eriko, Tadaka Etsuko. Effectiveness of the Online Daily Diary (ONDIARY) program on family caregivers of advanced cancer patients: A home-based palliative care trial. *Complementary Therapies in Clinical Practice 2022;*46: Article 101508

Abstract:

Objectives: There are many effective palliative care programs for patients with advanced cancer. However, little is known about effective programs for family caregivers of patients with advanced cancer, especially in home-based palliative care settings. This study aimed to determine the effect of the Online Daily Diary (ONDIARY) program on the quality of life (QOL) of family caregivers of patients with advanced cancer in home-based palliative care settings.

Methods: This study used a quasi-experimental design with a control group. The sample comprised 60 family caregivers (intervention group n = 30, control group n = 30) of patients with advanced cancer receiving home-based palliative care. The intervention group was assigned to the ONDIARY program in addition to usual care, and the control group was assigned to usual care. Group allocation was not randomized. The ONDIARY program is a 7-day online diary intervention program that aims to enhance emotional competence. Outcome measures were feasibility assessment, and primary and secondary outcome assessment. Primary and secondary outcome measures were the Caregiver Quality of Life Index-Cancer (CQOLC) and the six-item Kessler Psychological Distress Scale (K6). Repeated measures analysis of variance was performed on each measure, with group and group × time interactions.

Results: There was a significant group × time interaction in CQOLC scores ($F = 9.324$, $P = 0.003$). The CQOLC scores of family caregivers in the intervention group were maintained after the intervention, whereas those in the control group declined. There was no significant difference in K6 scores between the two groups.

Conclusion: The results suggest that the ONDIARY program in addition to usual care has potential to be effective in preventing decline and maintaining QOL of family caregivers of patients with advanced cancer in home-based palliative care settings.

Joshi Jyoti, Bandral Chetna, Manchanda Raj Kumar, Khurana Anil, Nayak Debadatta, Kaur Sukhbir. Evidence for Reversal of Immunosuppression by Homeopathic Medicine to a Predominant Th1-type Immune Response in BALB/c Mice Infected with Leishmania donovani. *Homeopathy 2022;* 111(1): 31-41p.

Abstract:

Background: Visceral leishmaniasis (VL) is a neglected tropical disease that is fatal if treatment is not given. The available chemotherapeutic options are unsatisfactory, and so complementary therapies like homeopathy might be a promising approach.

Methods: A nosode from a pure axenic culture of Leishmania donovani was prepared and screened for its anti-leishmanial potential both in an in-vitro and an in-vivo experimental approach.

Results: Leishmania donovani amastigote promastigote nosode (LdAPN 30C) exhibited significant anti-leishmanial activity against the promastigote forms of Leishmania donovani and was found to be safe. A study conducted on VL-infected mice revealed that LdAPN 30C resolved the disease by modulating the host immune response toward the Th1 type through upregulating the pro-inflammatory cytokines (IFN-γ and IL-17) and inducing nitric oxide (NO) levels in the infected macrophages. The hepatic parasite load was also found to be significantly decreased. The nosode was found to be safe, as no histological alterations in the liver or kidney were observed in the animals treated with the LdAPN 30C.

Conclusion: This is the first study in which an axenic culture of Leishmania donovani has been used for the preparation of a homeopathic medication. The study highlights the anti-leishmanial and immunomodulatory potential of a homeopathic nosode in experimental VL.

Kobayashi Akiko, Nagashima Keiko, Hu Ailing, Harada Yoshinao, Kobayashi Hiroyuki. Effectiveness and safety of kamikihito, a traditional Japanese medicine, in managing anxiety among female patients with intractable chronic constipation. *Complementary Therapies in Clinical Practice 2022;*46: Article 101526

Abstract:

Background and purpose: The prevalence of anxiety in patients with chronic constipation is particularly high and these individuals are not necessarily satisfied by normal treatments targeting the gastrointestinal tract. Kamikihito, a traditional Japanese Kampo medicine, has been widely used to date in treating anxiety and neurosis in Japan. We conducted a single-arm, open-label pilot study of female patients with intractable chronic constipation and anxiety who took kamikihito by mouth for 12 weeks.

Materials and methods: Validated symptom questionnaires on anxiety and gastrointestinal symptoms [the Profile of Mood States, second edition

(POMS2); the State–Trait Anxiety Inventory (STAI); and the Gastrointestinal Symptom Rating Scale (GSRS)] were completed at each study visit. Plasma, salivary, and stool samples were also assessed to evaluate levels of clinical bioactive substances linked to stress and inflammation, oxidative levels, the metabolome profile, and gut microbiota.

Results: Twenty-four patients completed this study. Anxiety was significantly reduced at four and 12 weeks (Tension–Anxiety subscale of the POMS2, $p = 0.006$ and $p = 0.039$; Trait anxiety score of the STAI, $p < 0.001$ and $p = 0.034$), while the total GSRS score was improved at 12 weeks ($p = 0.039$). Targeted metabolomics in plasma showed significant alterations in some metabolites associated with psychological symptoms, such as O-phosphoethanolamine. No significant differences were found between pre- and posttreatment levels of clinical bioactive substances related to stress and inflammation, oxidative levels, and the gut microbiota in this cohort. No serious adverse events occurred.

Conclusion: Kamikihito ameliorated psychological and gastrointestinal symptoms in patients with chronic constipation. In parallel with the onset of efficacy, kamikihito modulated some anxiety-related metabolites. Kamikihito was safe and well-tolerated.

Kriegman Orion. Boston Food Forest Coalition: Uniting Nature and Neighborhoods. *Integrative and Complementary Therapies 2022;*28(1): 12-16p.

Kurd R, Freed Y, Jarjoui A, Izbicki G, Levin P, Helvitz Y et al. Homeopathic Treatment for COVID-19-Related Symptoms: A Case Series. *Complementary Medicine Research 2022;*29(1): 83-88p.

Kus S, Immich G, Oberhauser C, Frisch D, Schuh A. Evaluating the Effectiveness of a One-Week Multimodal Prevention Program for Slowing down and Stress Reduction Performed in a German Health Resort: Results of a Randomized Controlled Trial. *Complementary Medicine Research 2022;*29(1): 6-16p.

Abstract:

Background: Effective concepts are required to overcome the negative impact of daily stressful overwhelming. We investigated the effectiveness of a 1-week multimodal program for stress reduction.

Methods: We performed a randomized controlled trial including adults with above-average stress level. The intervention consisted of health coaching, relaxation, physical activity, and balneotherapeutic elements. Individuals were randomized either to the intervention group (IG) or to one of the two control groups B and C. The main outcome was change in stress (Perceived Stress Questionnaire [PSQ], Screening Scale of Chronic Stress of the Trier Inventory for Chronic Stress [TICS-SSCS]) at 6 months post intervention; further outcomes were well-being (World Health Organization 5-Item Well-

Being Index [WHO-5]) and health status (EuroQol visual analog scale [EQ-5D VAS]). Data were collected pre/post intervention as well as after 1, 3, and 6 months.

Results: Data of 96 individuals (mean age 48.0 years, 74% female) were available for analyses. The IG improved overtime with –13.45 points for the PSQ and –6.44 points for the TICS-SSCS after 6 months. At 6-month follow-up the IG did not significantly differ from group B (PSQ: p = 0.2332; TICS-SSCS: p = 0.0805) or group C (PSQ: p = 0.0950; TICS-SSCS: p = 0.0607) when controlling for baseline (ANCOVA). Compared to group C, ANCOVA revealed significant differences in WHO-5 (p = 0.0292) and EQ-5D VAS (p = 0.0177) post intervention. At the 3- and 6-month follow-up and compared to group B, no substantial differences could be found for WHO-5 and EQ-5D VAS. Conclusion: The results indicate that even a short-term multimodal program for stress reduction appears to set a positive trend towards less perceived and chronic stress.

Lee Seoyoung, Choi Dha Hyun, Hong Minyoung, Lee In Seon, Chae Younbyoung. Open-Label Placebo Treatment for Experimental Pain: A Randomized-Controlled Trial with Placebo Acupuncture and Placebo Pills. *Journal of Integrative and Complementary Medicine 2022;*28(2): 136-45p.

Abstract:

Objective: An open-label placebo (OLP) is a placebo treatment in which the patient is aware that the treatment is a placebo. OLPs are considered effective for reducing pain, and previous studies have shown a stronger placebo effect for placebo acupuncture than for placebo pills. In this study, the authors compared the analgesic effects of OLP pills, OLP acupuncture, and a no treatment condition in healthy participants, and then examined the factors contributing to the OLP effect.

Design: Randomized controlled crossover trial.

Settings/Location: College of Korean Medicine, Kyung Hee University, Seoul, Republic of Korea.

Subjects: 34 healthy participants.

Intervention: Participants received three different treatments ("OLP-pill," "OLP-acupuncture," and "no treatment") on three separate days in random order.

Outcome Measurements: Before and after the treatment, heat pain stimuli were applied to the participants' hands, and pain tolerance, intensity, and unpleasantness were measured using a visual analog scale (range, 0–10).

Results: Data of 31 participants were included in the analysis. The authors found significant analgesic effects of the placebo pill and placebo

acupuncture in the OLP condition. Regression analyses revealed that expectations regarding treatment and practitioner identity influenced the analgesic effects of OLP acupuncture. There was no adverse event.

Conclusions: Expectations regarding treatment and practitioner identity influenced the analgesic effect of placebo acupuncture without deception. These findings provide new information regarding the cognitive factors underlying pharmacologic and nonpharmacologic treatments.

Li Si Hui, Hu Wei Shang, Wu Qiao Feng, Jun Gang Sun. Efficacy of bloodletting therapy in patients with acute gouty arthritis: A systematic review and meta-analysis. *Complementary Therapies in Clinical Practice 2022;*46: Article 101503

Abstract:

Background: Bloodletting therapy (BLT) is widely used to relieve acute gouty arthritis (AGA). However, limited evidence-based reports exist on the effectiveness and safety of BLT. This systematic review aims to evaluate the feasibility and safety of BLT in treating AGA.

Methods: Seven databases were exhaustively screened from the date of establishment to July 31, 2020, irrespective of the publication source and language. The included articles were evaluated for bias risk by using the Cochrane risk of bias assessment tool. All statistical analyses were done with Review Manager 5.3.

Results: Twelve studies involving 894 participants were included for the final analysis. Our meta-analysis revealed that BLT was highly effective in relieving pain (MD = −1.13, 95% CI [-1.60, −0.66], P < 0.00001), with marked alterations in the total effective (RR = 1.09, 95% [1.05, 1.14], P < 0.0001) and curative rates (RR = 1.37, 95%CI [1.17, 1.59], P < 0.0001). In addition, BLT could dramatically reduce serum C-reactive protein (CRP) level (MD = −3.64, 95%CI [-6.72, −0.55], P = 0.02). Both BLT and Western medicine (WM) produced comparable decreases in uric acid (MD = −18.72, 95%CI [-38.24, 0.81], P = 0.06) and erythrocyte sedimentation rate (ESR) levels (MD = −3.01, 95%CI [-6.89, 0.86], P = 0.13). Lastly, we demonstrated that BLT was safer than WM in treating AGA (RR = 0.36, 95%CI [0.13, 0.97], P = 0.04).

Conclusion: BLT is effective in alleviating pain and decreasing CRP level in AGA patients with a lower risk of evoking adverse reactions.

Liao Jian An, Yeh Yuan Chieh, Chang Zi Yu. Efficacy and safety of traditional Chinese medicine Guilu Erxian Jiao in the treatment of knee osteoarthritis: A systematic review and meta-analysis. *Complementary Therapies in Clinical Practice 2022;*46: Article 101515

Abstract:

Objective: A systematic review was conducted to investigate the efficacy of Guilu Erxian Jiao (GEJ) in the treatment of knee osteoarthritis (OA).

Methods: We searched PubMed, MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, Chinese Electronic Periodical Services, and ClinicalTrials.gov to identify relevant randomized controlled trials or controlled clinical trials, from the inception of each source to April 20, 2021. Primary outcome included overall efficacy, pain score, and Lequesne index score; secondary outcome included adverse events. Methodological quality was assessed using the Cochrane risk of bias tool (RoB 1.0). The meta-analysis was performed based on a random-effects model due to anticipated clinical heterogeneity. The grading of overall evidence was assessed using the GRADE system. The study protocol was registered on PROSPERO (CRD42021233573).

Results: Eight studies were included. Compared to controls, GEJ exhibited superior overall efficacy for treating OA (risk ratio (RR) = 1.20; 95% confidence interval (CI) = 1.06–1.35). Regarding pain score, there was no statistical difference between GEJ and controls (standardized mean difference (SMD) = 0.27; 95% CI = −0.91 – 1.46). No significant difference was found in Lequesne score between GEJ and controls (MD = −0.25; 95% CI = −0.52 – 0.01). No statistical difference in adverse reactions was observed between GEJ and controls (risk difference (RD) = −0.01; 95% CI = −0.05–0.03).

Conclusion: Our findings suggest that GEJ may have positive effects on overall efficacy in treating OA. However, there is insufficient evidence regarding pain score, Lequesne score, and knee joint function score.

Loureiro APC, Burkot J, Oliveira J, Barbosa JM. WATSU therapy for individuals with Parkinson's disease to improve quality of sleep and quality of life: A randomized controlled study. *Complementary Therapies in Clinical Practice 2022;*46: Article 101523

Abstract:

Background and Purpose: Sleep disorders are one of the most frequent non-motor symptoms of Parkinson's disease (PD). This study aimed to verify whether adding WATSU to land-based therapy leads to additional beneficial therapeutic effects regarding quality of sleep and quality of life (QOL) in individuals with PD.

Materials & methods: A randomized control trial design was used. Participants completed nine-week interventions. The control group (CG) received land-based therapy, while the intervention group (IG) received the same land-based therapy and additionally WATSU. Sleep quality and QOL were measured at baseline and post-interventions by Pittsburgh Sleep Quality Index and Nottingham Health Profile, respectively.

Results: Twenty-eight participants completed the study. In contrast to CG, the IG presented with significant improvements in both, quality of sleep and QOL ($p < 0.001$).

Conclusion: WATSU has the potential to be an attractive adjunct therapy for producing positive health impacts regarding sleep quality, which may translate to an overall improvement in QOL of individuals with PD.

Love Lamara, Anderson Avery M, Sadovszky Victoria von, Kusiak Julie, Noritz Garey. Study of Reiki therapy on unpleasant symptoms in children with cerebral palsy. *Complementary Therapies in Clinical Practice 2022;*46: Article 101529

Abstract:

Children with Cerebral Palsy (CP) commonly experience unpleasant symptoms such as pain, anger, and sadness. The purpose of this quasi-experimental study, guided by the Theory of Unpleasant Symptoms (TOUS), was to examine the practicality and impact of delivering Reiki Therapy (RT) in homes over an 8-week intervention phase to children with CP. Thirteen pediatric participants were recruited, ranging in age from 5 to 16 years. Reiki Therapy was administered by a Level 3 Reiki Therapist in the home for 8 consecutive weeks. Parents completed on-line questionnaires addressing their children's unpleasant symptoms. Hair cortisol was measured as an indicator of stress. Nearly all study procedures were completed by the participants, indicating that the methods are feasible for a larger study. Reiki Therapy significantly decreased pain while lying down (3.09 vs. 2.00; $p = .002$) but not while sitting (2.55 vs. 2.09; $p = .40$). Anger symptoms showed a trend towards improvement in the participants. These preliminary findings demonstrate that Reiki is a therapeutic modality worthy of further investigation in the CP pediatric population.

Lucas Martha. Clinician Wellness: Self-Care for Staying Healthy: Using Chinese Medicine to Help Prevent Depression and Other Mental Health Issues. *Integrative and Complementary Therapies 2022;*28(1): 17-19p.

Lucius Khara. Diet and Nutritional Supplements for Psoriasis. *Integrative and Complementary Therapies 2022;*28(1): 43-50p.

Abstract:

Psoriasis is a chronic inflammatory condition that typically presents with papulosquamous scaling dermatitis. While psoriasis' most visible effects are related to the skin, this condition involves inflammation at a more systemic level as well. Psoriasis is also associated with gut dysbiosis. This article reviews both dietary interventions and nutritional supplements that have been studied for their effects on psoriasis. This includes vitamin D, fish oil, antioxidants, curcumin, and probiotics. Many of these substances may impact psoriasis by modulating the microbiome or exerting anti-inflammatory effects.

Manchanda Raj Kumar, Gupta Meeta, Gupta Ankit, Haselen Robbert van. Clinical and Biological Effects of Homeopathically Prepared Signaling Molecules: A Scoping Review. ***Homeopathy 2022;*** **111(1): 10-21p.**

Abstract:

Background: Signaling molecules such as cytokines and interleukins are key mediators for the immune response in responding to internal or external stimuli. Homeopathically prepared signaling molecules have been used therapeutically for about five decades. However, these types of products are not available in many countries and their usage by homoeopaths is also infrequent. The aim of this scoping review is to map the available pre-clinical and clinical data related to the therapeutic use of homeopathically prepared signaling molecules.

Methods: We conducted a scoping review of clinical and pre-clinical studies of therapeutically used signaling molecules that have been prepared in accordance with an officially recognized homeopathic pharmacopoeia. Articles in peer-reviewed journals reporting original clinical or pre-clinical research of homeopathically prepared signaling molecules such as interleukins, cytokines, antibodies, growth factors, neuropeptides and hormones, were eligible. Non-English language papers were excluded, unless we were able to obtain an English translation. An appraisal of eligible studies took place by rating the direction of the outcomes on a five-point scale. The quality of the papers was not systematically assessed.

Results: Twenty-eight eligible papers, reporting findings for four different manufacturers' products, were identified and reviewed. Seventeen papers reported pre-clinical studies, and 11 reported clinical studies (six experimental, five observational). A wide range of signaling molecules, as well as normal T-cell expressed specific nucleic acids, were used. A majority of the products (21 of 28) contained two or more signaling molecules. The most common clinical indications were psoriasis, vitiligo, rheumatoid arthritis, respiratory allergies, polycystic ovary syndrome, and herpes. The direction of the outcomes was positive in 26 papers and unclear in two papers.

Conclusion: This scoping review found that there is a body of evidence on the use of homeopathically prepared signaling molecules. From a homeopathy perspective, these substances appear to have therapeutic potential. Further steps to explore this potential are warranted.

Manchanda Raj Kumar, Miglani Anjali, Chakraborty Moumita, Meena Baljeet Singh, Sharma Kavita, Gupta Meeta et al. Impact of Bias in Data Collection of COVID-19 Cases. ***Homeopathy 2022;*** **111(1): 57-65p.**

Abstract:

Background: Prognostic factor research (PFR), prevalence of symptoms and likelihood ratio (LR) play an important role in identifying prescribing indications of useful homeopathic remedies. It involves meticulous unbiased collection and analysis of data collected during clinical practice. This paper is an attempt to identify causes of bias and suggests ways to mitigate them for improving the accuracy in prescribing for better clinical outcomes and execution of randomized controlled studies.

Methods: A prospective, open label, observational study was performed from April 2020 to December 2020 at two COVID Health Centers. A custom-made Excel spreadsheet containing 71 fields covering a spectrum of COVID-19 symptoms was shared with doctors for regular reporting. Cases suitable for PFR were selected. LR was calculated for commonly occurring symptoms. Outlier values with LR >5 were identified and variance of LRs was calculated.

Results: Out of 1,889 treated cases of confirmed COVID-19, 1,445 cases were selected for pre-specified reasons. Nine medicines, Arsenicum album, Bryonia alba, Gelsemium sempervirens, Pulsatilla nigricans, Hepar sulphuricus, Magnesia muriaticum, Phosphorus, Nux vomica and Belladonna, were most frequently prescribed. Outlier values and large variance for Hepar sulphuricus and Magnesia muriaticum were noticed as indication of bias. Confirmation bias leading to lowering of symptom threshold, keynote prescribing, and deficiency in checking of all symptoms in each case were identified as the most important sources of bias.

Conclusion: Careful identification of biases and remedial steps such as training of doctors, regular monitoring of data, checking of all pre-defined symptoms, and multicenter data collection are important steps to mitigate biases.

Mathie Robert T. Individualisation: The Heart of Homeopathy. ***Homeopathy 2022;*** **111(1): 1p.**

Munshi Renuka, Talele Gitanjali, Shah Rajesh. In-Vitro Evaluation of Antimicrobial Activities of Escherichia coli, Klebsiella pneumoniae,

Salmonella typhi, Neisseria gonorrhoeae, and Candida albicans Nosodes. *Homeopathy 2022;* 111(1): 42-48p.

Abstract:

Background: This study presents the results of the minimum inhibitory concentration (MIC) assay of a series of nosodes: namely Escherichia coli, Klebsiella pneumoniae, Salmonella typhi, Neisseria gonorrhoeae, and Candida albicans. Each was tested against its corresponding infection as well as cross infections.

Methods: In-vitro efficacy of polyvalent nosodes was tested using the MIC assay technique. The nosodes, namely C. albicans polyvalent nosode (35c, 100c), N. gonorrhoeae (35c), K. pneumoniae (35c, 100c), E. coli polyvalent nosode (35c, 100c) and Salmonella typhi polyvalent nosode (30c, 100c), were tested along with positive and negative controls. Nosodes were studied in different potencies and at 1:1 dilution.

Results: C. albicans polyvalent nosode 35c, 100c, N. gonorrhoeae 35c, and positive control amphotericin B showed inhibition of the growth of C. albicans species. K. pneumoniae 35c, E. coli polyvalent nosode 100c, and meropenem (positive control) showed inhibition of the growth of K. pneumoniae; this effect was not seen with ceftriaxone, ofloxacin and amoxicillin antibiotics. E. coli polyvalent nosode 30c in 10% alcohol (direct and dilution 1:1) and the positive controls ciprofloxacin, ofloxacin, and amoxicillin showed inhibition of the growth of E. coli. The S. typhi polyvalent nosode 30c in 10% alcohol showed inhibition of growth of S. typhi.

Conclusion: This study reveals that the tested nosodes exhibited antibacterial potential against the corresponding micro-organisms and against other selected organisms studied using this assay.

Piskorz Joanna, Fron Kamila, Hoppe Gosik Joanna, Czub Marcin. Challenging Case in Clinical Practice: Mindfulness, Slow Diaphragmatic Breathing and Virtual Reality Based Intervention for Chronic Pain. *Integrative and Complementary Therapies 2022;*28(1): 20-27p.

Redmond Rebecca, Steel Amie, Wardle Jon, Adams Jon. Naturopathy utilisation by Australian women with diagnosed endometriosis: A cross-sectional survey. *Complementary Therapies in Clinical Practice 2022;*46: Article 101539

Abstract:

Background and purpose: Endometriosis is a painful female reproductive disease resulting in unmet health needs. Women with endometriosis frequently access different types of health care, yet little is known about naturopathic use. The purpose of this study is to explore the naturopathic utilisation by women with endometriosis in Australia.

Materials and methods: This study reports a cross-sectional survey of Australian women with endometriosis. Participants were recruited through the not-for-profit organisations Endometriosis Australia and EndoActive social media platforms. Data was collected through a self-administered questionnaire by those eligible to participate. Participants were included if they self-reported a diagnosis of endometriosis via laparoscopic surgery and were an Australian resident.

Results: Of the recruited 303 women with endometriosis, 60 women reported consulting with a naturopath for endometriosis care. Women consulting with a naturopath, reported also consulting with a laparoscopic surgeon (66.7%, $p = 0.01$), acupuncturist (53.3%, $p \leq 0.01$), physiotherapist (41.7%, $p = 0.01$), nutritionists/dietitians ($n = 22$, 36.7%, $p = 0.01$) or homeopath (15.0%, $p \leq 0.001$), in addition to their naturopath in the previous 12 months for endometriosis management. Compared to non-naturopathic users, women reported frequently experiencing dyspareunia (OR 2.9, CI 1.4–5.9, $p = 0.002$) and reported a higher use of vitamin D supplementation for endometriosis management (OR 4.9, CI 2.5–9.9, $p \leq 0.001$).

Conclusion: Women who use naturopathy for endometriosis appear to be high users of health care services, both within complementary medicine and conventional medicine. The efficacy and role of naturopathic treatments and care for women with endometriosis requires further investigation.

Rodriguez Kerri E, Bibbo Jessica, O'Haire Marguerite E. Perspectives on facility dogs from pediatric hospital personnel: A qualitative content analysis of patient, family, and staff outcomes. *Complementary Therapies in Clinical Practice 2022;*46: Article 101534

Abstract:

An increasing number of children's hospitals feature full-time resident facility dogs, which are specially trained to work alongside pediatric healthcare professionals to improve the patient experience. This qualitative study aimed to describe the role that facility dogs play in the lives of patients, families, and hospital staff. A total of N = 73 pediatric healthcare professionals that worked with 46 facility dogs across 17 children's hospitals in the US completed a set of open-ended questions in an online survey. Responses were analyzed via a conventional thematic analysis and organized into themes and sub-themes. Facility dogs were described to benefit pediatric healthcare professionals' daily lives through improving stress and wellbeing, staff relationships, and job-related morale. Negative

impacts included increased burdens and responsibilities in the workplace. Facility dogs were also described to benefit patients and families by helping build rapport, providing a comforting presence and positive resource, and normalizing the hospital environment. In conclusion, facility dog programs were found to be a promising complementary intervention to benefit both staff as well as and patients and families. Future research is warranted to examine short-term and long-term implications of facility dog programs for staff, patient, and family wellbeing.

Rotter G, Binting S, Tissen Diabate T, Ortiz M, Brinkhaus B. Osteopathic Medicine in Four Chronic Musculoskeletal Pain Diseases: An Observational Trial with Follow-Up. *Complementary Medicine Research 2022;*29(1): 53-66p.

Abstract:

Background and Aim: Patients with chronic musculoskeletal pain diseases (CMPDs) often use osteopathic medicine (OM), although the changes in patients with pain diseases are still insufficiently investigated. This study aimed to observe changes along and after OM in addition to routine care on pain, functioning, and quality of life in patients with four CMPDs.

Methods: In this observational trial with follow-up, patients suffering from chronic neck pain (CNP, n = 10), chronic low back pain (CLBP, n = 10), chronic shoulder pain (CSP, n = 10), or chronic knee pain (CKP, n = 10) received up to six OM sessions in addition to routine care.

Results: A total of 40 patients (73% female, mean age 47.7 ± 8.3 years, mean pain intensity 59.4 ± 12.5 mm, measured by a visual analog scale [VAS] 0–100 mm) were included. After 26 weeks, there was an improvement in the VAS pain score in the whole population (mean difference to baseline –33.1 mm [95% CI –40.5 to –25.7]), as well in the patients with the four diseases: CNP (–33.7 mm [–54.7 to –12.6]), CLBP (–28.2 mm [–47.9 to –8.4]), CSP (–32.4 [–46.8 to –18.0]), and CKP (–38.1 mm [–49.1 to –27.0]). Regarding disease-specific outcomes, we found improvements in CNP, as measured by the neck disability index (scale 0–50; mean difference –3.6 [–9.0 to 1.9]), CLBP, as measured by the low back pain rating scale (scale 0–60; –3.4 [–12.5 to 5.7]), CSP, as measured by the disabilities of the arm, shoulder and hand score (scale 0–100; –13.4 [–23.1 to –3.7]), and CKP, as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (scale 0–96; –13.0 [–23.5 to –2.5]). These improvements persisted through week 52. No adverse events were observed.

Conclusion: The study observed beneficial changes along and after the OM treatment in addition to routine care in patients with four different CMPDs. High-quality, multicenter randomized controlled trials are strongly needed to compare the effectiveness of OM and standard care interventions in treating CMPDs in the future. We have provided sufficient data for sample size calculations for these trials.

Rountree Robert. Integrative Rheumatology and Environmental Health. *Integrative and Complementary Therapies 2022;*28(1): 1-11p.

Sahraei Farideh, Rahemi Zahra, Sadat Zohreh, Zamani Batool, Mianehsaz Elaheh. Effect of Swedish massage on pain in rheumatoid arthritis patients: A randomized controlled trial. *Complementary Therapies in Clinical Practice 2022;*46: Article 101524

Abstract:

Background and Purpose: Joint pain is one of the most common symptoms in rheumatoid arthritis patients and require medical attention. The purpose of this study was to assess the effects of Swedish massage on pain and painkiller consumption in rheumatoid arthritis patients.

Materials and methods: A total of 60 patients participated in the experiment, with half assigned to the control group (n = 30) and half to the experimental (n = 30) group using the block randomization method. On patients in the experimental group, a 30-min Swedish massage was performed regularly for eight weeks: twice a week for the first four weeks, and three times a week for the last four weeks. The control group received routine care. The visual analogue scale-pain was used to measure pain in the two groups at three points of time: before the beginning of the experiment, immediately after the last session, and one month after the last session of the intervention.

Results: The analysis of covariance showed that there were significant differences between the two groups' mean scores of pain and painkiller consumption immediately after and one month after the last session of the intervention ($p = 0.01$). Furthermore, in the experimental group, the mean scores of pain and painkiller consumption decreased over the three points of time ($p < 0.05$).

Conclusion: Swedish massage can be effective in reducing pain and the need to use painkillers in rheumatoid arthritis patients.

Sanchez Francisca A, Rosales Javiera R, Godoy Pablo R, Barria R Mauricio. Effects of inhalation aromatherapy as a complementary therapy in pediatric patients in the clinical practice: A systematic review. *Complementary Therapies in Clinical Practice 2022;*46: Article 101516

Abstract:

Background: Inhalation aromatherapy is a complementary therapy in different clinical settings, but there is little evidence about its effectiveness in childcare.

Objective: To assess the effectiveness of inhalational aromatherapy in the care of hospitalized pediatric patients.

Methods: Systematic review of clinical trials and quasi-experimental studies, based on PRISMA recommendations, searching Medline, Web of Science, Scopus, SciELO, LILACS, CINAHL, Science Direct, EBSCO, and updated databases. The Down and Black 2020, RoB 2020 CLARITY, and ROBINS-I 2020 scales were used through the Distiller SR software to verify the studies' internal validity and risk of bias.

Results: From 446 articles identified, 9 fulfilled the inclusion criteria. Seven were randomized controlled trials (RCTs), one pilot RCT, and one non-randomized quasi-experimental trial.

Different outcomes were analyzed, with pain being the most frequently measured variable. None of the 6 studies that evaluated pain showed significant effects with inhalation aromatherapy. Additionally, non-significant effects were found regarding nausea, vomiting, and behavioral/emotional variables.

Conclusions: The findings are still inconclusive, and more evidence is required from future studies with high methodological quality, blinding, and adequate sample sizes.

Santana Tamires Miranda, Ogawa Lucas Yuiiti, Rogero Marcelo Macedo, Barroso Lucia Pereira, Castro Inar Alves de. Effect of resveratrol supplementation on biomarkers associated with atherosclerosis in humans. *Complementary Therapies in Clinical Practice 2022;*46: Article 101491

Abstract:

Previous studies have suggested the beneficial effects of resveratrol against cardiovascular disease (CVD). However, there are inconsistent results on cardiovascular-related biomarkers mainly because of variable dosage, intervention time and baseline characteristics of the population. Thus, the exact effect of resveratrol remains unclear. We conducted a review to classify the studies that applied resveratrol to supplement humans according to the major biomarkers and identify which protocol characteristics would be associated with each result profile. Randomized clinical trials that assessed resveratrol effect on biomarkers related to atherosclerosis were searched in databases. Biochemical data were collected from 27 studies on the baseline and post-intervention time. We selected 12 biomarkers to compose the matrix, based on their clinical relevance and higher variation level. A total of 32 assays were obtained from these 27 studies. The net change (%) was calculated for each biomarker. Applying multivariate analysis, the assays were grouped into 3 clusters. Studies that composed Cluster II were characterized by a mean dose of 454.14 mg/day for 74.21 days and showed higher reduction of triglyceride concentration and blood pressure, while those composing Cluster III applied doses around 273.75 mg/day for about 175.33 days and showed the highest HDL increase. Thus, interventions with resveratrol could be customized according to the patient condition, in terms

of “dose/time of intervention”. This information can be applied to combine resveratrol with drugs to reduce blood pressure or improve lipid profile in further clinical studies.

Santiago Rui Jose, Esteves Jorge Eduardo, Baptista Joao Santos, Magalhaes Andre, Costa Jose Torres. Results of a feasibility randomised controlled trial of osteopathy on neck-shoulder pain in computer users. *Complementary Therapies in Clinical Practice 2022;*46: Article 101507

Abstract:

Background: Computer use is a well-known source of chronic pain, leading to absenteeism and reduced productivity and well-being. This study evaluated the feasibility of conducting a full-scale randomised controlled trial. Several methodological variables defined trial feasibility.

Materials and methods: Thirty adults, daily computer users reporting pain, were recruited. Data collection took place at LABIOMEP. Participants were randomised into 1 of 3 parallel groups and received either osteopathic, sham or no treatment. Only the volunteers were blind to group assignments. The primary objective was to study the feasibility and acceptability of the protocol.

Results: Of 77 participants interested, 30 were included and randomised into three groups of ten. All participants concluded the study, and all the data was analysed. The feasibility outcomes were deemed appropriate. No adverse events or severe side effects were reported or identified.

Conclusion: Studying the efficacy of osteopathic consultation on computer users by conducting an RCT is feasible and safe. With adjustments, a full-scale study can be designed.

Trial registration: ClinicalTrials.gov with the identifier: NCT04501575. Date registered August 06, 2020.

Saumaa Hiie. Anxiety and Somatic Dance. *Integrative and Complementary Therapies 2022;*28(1): 39-42p.

Schibel S, Steinert M, Matthes H, Grah C. Complementary Anthroposophical Program for the Palliative Treatment of Lung Cancer: Rationale and a Randomized Feasibility Study. *Complementary Medicine Research 2022;*29(1): 27-34p.

Abstract:

Background: Lung cancer is the oncological disease with the highest mortality worldwide. Health-related quality of life is severely compromised in the majority of patients. While the efficacy of early palliative psychosocial therapy has been demonstrated in several recent studies, appropriate

therapy modules could so far not be integrated into daily practice of care. Therefore, an additive multimodal treatment concept for oncological centers was drafted: the Additive anthroposophic integrative medicine Cancer Concept of Early supportive or Palliative lung cancer Treatment (ACCEPT®).

Patients and Methods: The first module consisted of a 3-month health education program, the second module was a concept of psychosocial interventions, and the third module was a supervised home training program. Between 2017 and 2018, 20 lung cancer patients (UICC IIIB/IV) were included and randomly assigned to treatment (n = 10) or a waiting control group (n = 10). The treatment group started ACCEPT® for 3 months immediately after diagnosis and received also standard oncological care (SOC) while the waiting control group received SOC only for 3 months, followed by ACCEPT® after this period. Health-related quality of life, disease management, disease-specific symptoms, and feasibility of the ACCEPT® were monitored at 4 time points.

Results: 7 out of 10 patients in the treatment group (3 dropped out) and 6 out of 10 in the waiting control group (4 died during the intervention) completed treatment.

Discussion/Conclusion: Lung cancer patients with high symptom load may benefit from ACCEPT®. The feasibility of this adjunctive therapy was demonstrated. The combination of SOC and ACCEPT® is feasible and applicable to a heterogeneous patient group and should be further evaluated with respect to efficacy and dosing.

Schitter Agnes M, Radlinger Lorenz, Kurpiers Nicolas, Frei Peter. Application areas and effects of aquatic therapy WATSU: A survey among practitioners. *Complementary Therapies in Clinical Practice 2022;*46: Article 101513

Abstract:

Introduction: WATSU (WaterShiatsu) is a treatment administered in warm water. The present study investigated if and how frequently scientifically studied application areas and effects of WATSU occur in practice, whether similar effectiveness of WATSU is observed in trials and practice, and whether practitioners can contribute additional application areas and effects of WATSU.

Methods: Application areas and effects of WATSU reported in a recent systematic review were extracted verbatim to be assessed in a worldwide multilingual cross section online survey, generating quantitative and qualitative data. A pre-test and retest were conducted to ensure quality and evaluate the questionnaire's psychometric properties.

Results: Answers of 191 respondents were processed. All proposed 26 application areas and 20 effects were confirmed, each with relatively high

ratings of observed effectiveness of WATSU. WATSU was frequently applied in healthy individuals (including during pregnancy), and individuals in various pain- (e.g., low back pain, neck pain, myofascial pain, fibromyalgia) and stress-related (e.g., stress, depression, sleep disorders, fatigue, anxiety disorders) conditions. Frequently confirmed effects were physical relaxation, relief of physical tension, pain relief, increased mobility and flexibility, improved quality of life, spiritual experiences, and increased psychological health. Respondents contributed 73 additional application areas and effects (both, mental and physical) of WATSU.

Conclusions: Application areas and effects of WATSU are consistently employed practically and scientifically. Respondents' ratings of effectiveness of WATSU match tentative research efforts. WATSU is cautiously recommended for the use in pain- and stress-related conditions. Short- and long-term effectiveness of WATSU need to be evaluated in high level intervention studies.

Sekar Bhuvaneswari Rajachandra, Nair Janardanan Kainikkara Raghavan, Sunny Anita, Manoharan Amrutha. Individualised Homeopathic Medicine in the Treatment of Infertility: A Case Series. ***Homeopathy 2022;*** **111(1): 66-73p.**

Abstract:

Background: Infertility is the inability of a person to conceive despite having carefully timed, unprotected sexual intercourse for 2 years. There are 80 to 168 million people worldwide who are suffering from infertility, resulting in feelings of failure, embarrassment or personal disappointments, which in turn lead to strained relationships with the spouse, family, and social circle. This study aimed to highlight the significance of using individualised homeopathic medicine in the treatment of infertility. In this study, seven couples suffering from infertility, who conceived after undergoing treatment at the National Homoeopathy Research Institute in Mental Health, Kottayam, were included.

Methods: Significant improvement within a short period of treatment and the combined co-operative response from both partners were the key considerations for our selection of these seven cases from 12 successfully treated cases out of 20 couples in total. Detailed case studies were achieved for all seven couples. The individualised homeopathic medicines were prescribed after repertorisation based on confirmation with the authorised textbooks of Materia Medica. All couples were followed up on a monthly basis, and outcome measures of positive pregnancy (i.e., urine pregnancy test and ultrasonography of the pelvis) were evaluated.

Results: All seven couples successfully conceived. Two of the couples showed a significant improvement of underlying symptoms within 2 months, whereas three responded within the third month of treatment. One of the couples conceived in the fourth month and the seventh couple took 8 months to have a successful pregnancy.

Conclusions: Overall, the results of the case series indicate that individualised homeopathic medicines are useful in the management of infertility.

Shahid Sana, Ghosh Shubhamoy, Chakraborty Ardhendu Shekhar, Maiti Shukdeb, Sadhukhan Satarupa, Koley Munmun et al. Efficacy of Individualized Homeopathic Medicines in Plantar Fasciitis: Double-blind, Randomized, Placebo-Controlled Clinical Trial. ***Homeopathy 2022;*** **111(1): 22-30p.**

Abstract:

Introduction: Plantar fasciitis (PF) is a chronic degenerative condition causing marked thickening and fibrosis of the plantar fascia, and collagen necrosis, chondroid metaplasia and calcification. There is little convincing evidence in support of various approaches, including homeopathy, for treating PF. This study was undertaken to examine the efficacy of individualized homeopathic medicines (IHMs) compared with placebo in the treatment of PF.

Methods: A double-blind, randomized, placebo-controlled trial was conducted at the outpatient departments of Mahesh Bhattacharyya Homoeopathic Medical College and Hospital, West Bengal, India. Patients were randomized to receive either IHMs or identical-looking placebo in the mutual context of conservative non-medicinal management. The Foot Function Index (FFI) questionnaire, as an outcome measure, was administered at baseline, and every month, up to 3 months. Group differences (unpaired t-tests) and effect sizes (Cohen's d) were calculated on an intention-to-treat sample. The sample was analyzed statistically after adjusting for baseline differences.

Results: The target sample size was 128; however, only 75 could be enrolled (IHMs: 37; Placebo: 38). Attrition rate was 9.3% (IHMs: 4, Placebo: 3). Differences between groups in total FFI% score favored IHMs against placebo at all the time points, with large effect sizes: month 1 (mean difference, -10.0; 95% confidence interval [CI], -15.7 to -4.2; p ¼ 0.001; d ¼ 0.8); month 2 (mean difference, -14.3; 95% CI, -20.4 to -8.2; p <0.001; d

¼ 1.1); and month 3 (mean difference, 23.3; 95% CI, -30.5 to -16.2; p <0.001; d ¼ 1.5). Similar significant results were also observed on three FFI sub-scales (pain%, disability%, and activity limitation%). Natrum muriaticum (n ¼ 14; 18.7%) and Rhus toxicodendron and Ruta graveolens (n ¼ 11 each; 14.7%) were the most frequently prescribed medicines. No harms, serious adverse events, or intercurrent illnesses were recorded in either of the groups.

Conclusion: IHMs acted significantly better than placebo in the treatment of PF; however, the trial being underpowered, the results should be interpreted as preliminary only. Independent replications are warranted.

Sharma Piyush, Yadav Raj Kumar, Khadgawat Rajesh, Dada Rima. 12-Week Yoga-Based Lifestyle Intervention Might Positively Modify Cellular Aging in Indian Obese Individuals: A Randomized-Controlled Trial. *Journal of Integrative and Complementary Medicine 2022;*28(2): 168-78p.

Abstract:

Background: Telomeres and telomerase are considered cardinal biomarkers of cellular aging. Shorter telomeres and low telomerase activity have been associated with obesity and accelerated aging.

Objective: To compare the effects of a yoga-based lifestyle intervention (YBLI) with the standard of care (SOC) on cellular aging by estimating telomere length (TL) and telomerase activity in obesity.

Design and setting: A parallel, two-arm, randomized-controlled trial was conducted at the Integral Health Clinic, Department of Physiology, All India Institute of Medical Sciences, New Delhi, from March 2017 to October 2019.

Participants: Obese (n = 72), body mass index (BMI), 25–35 kg/m2, aged 20–45 years, male (21), and female (51).

Intervention: Seventy-two obese participants were randomized to receive either a 12-week SOC (n = 36) or YBLI (n = 36). SOC included management of obesity as per Indian guidelines including a hypocaloric individualized diet and physical activity. The pretested YBLI included asana (physical postures), pranayama (breathing exercises), and meditation.

Methods: Blood samples were collected from both the groups at baseline, 2, 4, and 12 weeks. DNA was extracted from peripheral blood mononuclear cells. TL was measured by quantitative PCR, and serum telomerase levels by immunoassay.

Outcome measures: Primary outcome measures were the changes in the TL and telomerase levels between the two groups at week 12. Secondary

outcome measures were the changes in TL and telomerase, and anthropometric parameters (body weight, BMI, waist-to-hip ratio) at 2, 4, and 12 weeks of intervention in both SOC and YBLI groups.

Results: There were no significant changes in TL and telomerase levels between the groups at week 12. The TL was significantly greater in the YBLI group versus the SOC group ($p < 0.0001$) at 2 weeks. The anthropometric and physiological parameters were influenced positively by both SOC and YBLI.

Conclusion: The study did not meet the primary objective, although the results are suggestive of a positive impact of YBLI on aging in obesity as noted within the YBLI group. However, the results should be interpreted carefully, and in the light of other published data. Larger studies to better understand the possible positive benefits of YBLI on cellular aging are recommended. Clinical Trail Registration No. CTRI/2016/08/007136.

Sharma Sachin Kumar, Telles Shirley, Gandharva Kumar, Balkrishna Acharya. Yoga instructors' reported benefits and disadvantages associated with functioning online: A convenience sampling survey. *Complementary Therapies in Clinical Practice 2022;*46: Article 101509

Abstract:

Background: Among numerous changes in response to the COVID-19 pandemic, most yoga classes have repositioned online. However benefits, difficulties and satisfaction of teaching yoga online remain to be studied. With this background the present survey aimed to determine: (i) benefits, disadvantages and satisfaction of teaching yoga online and (ii) their association with characteristics related to (a) socio-demographic, (b) online yoga teaching experience and (c) yoga practice.

Methods: Three hundred and five yoga instructors were invited to take part in the online survey. Of these, 181 (m:f = 98:83) responded to the survey satisfactorily and were included.

Results: The three most common benefits of teaching yoga online were: (i) a sense of safety from risk of COVID-19 (93.92%), (ii) cost saving (82.87%) and (iii) wider access to trainees within India (77.90%). The three most common disadvantages were: (i) technical difficulties (74.03%), (ii) missing in-person contact (63.90%) and (iii) concern that online instructions can lead to injury (59.16%). Around 66.30% respondents were satisfied with the monitoring of trainees during online yoga classes while 70.16% respondents were satisfied with the level of attention they could pay to the topic they were teaching during online yoga class. The benefits and disadvantages of teaching yoga online varied with the characteristics of yoga instructors ($p < 0.05$, $x2$ test).

Conclusions: The benefits and disadvantages of teaching yoga online are of relevance during and beyond the pandemic. Characteristics related to (i) socio-demographics, (ii) online yoga teaching and (iii) yoga practice influence reported benefits and disadvantages of teaching yoga online.

Soleimani Mohsen, Kashfi Leyla Sadat, mirmohamadkhani Majid, Ghods Ali Asghar. Effect of aromatherapy with peppermint essential oil on anxiety of cardiac patients in emergency department: A placebo-controlled study. *Complementary Therapies in Clinical Practice 2022;*46: Article 101533

Abstract:

Introduction: Anxiety is an unpleasant feeling that increases the myocardial oxygen demand in acute coronary syndrome. This study aimed to evaluate the effect of peppermint aromatherapy on anxiety in patients with acute coronary syndrome in the emergency department.

Materials and methods: In this clinical trial study, 64 patients with acute coronary syndrome were randomly divided into intervention and control groups. In the intervention group, a cotton ball was soaked in 100% peppermint essential oil and placed about 20 cm from the patient's nose for 1 h while in the control group, the cotton ball was soaked in water. Anxiety was measured before and after the intervention with The Spielberger state-trait anxiety inventory. The data were analyzed in SPSS ver.23 software.

Results: No significant difference was observed between the two groups in terms of patients' demographic data. The mean score of trait and state anxiety before the intervention was not significantly different between the two groups. After the intervention, anxiety was significantly lower in the intervention group (37.72 ± 10.41) compared to the control group (42.62 ± 5.99) ($P = 0.021$). Results indicated a significant decrease in anxiety after the intervention ($P < 0.001$) in the intervention group. Such a difference was not significant in the control group.
Conclusion: Peppermint essential oil inhalation significantly reduces anxiety of patients with acute coronary syndrome in emergency department.

Stensland Meredith L, McGeary Don D. Use of animal-assisted interventions in relieving pain in healthcare settings: A systematic review. *Complementary Therapies in Clinical Practice 2022;*46: Article 101519

Abstract:

Background and objective: Therapeutic interaction with animals for patients coping with physical and mental health conditions is a growing interest among healthcare providers and researchers. We aimed to comprehensively summarize and evaluate the current state of evidence examining the use of animal-assisted interventions [AAI] for pain relief in healthcare settings.

Design: Systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.

Methods: Two researchers independently assessed publications dated before February 5, 2021 in OVID Medline, CINAHL, and PsychINFO databases, and used the Delphi list to evaluate the quality of the evidence.

Results: Of the 109 studies screened, a total of 24 studies totaling 1,950 participants were ultimately included. Studies varied in design, including single group trials (8), controlled trials with at least two groups (6), and randomized controlled trials (10). The most common form of pain measurement was the visual or numeric rating scale. For the 18 studies that reported data on changes in pain severity from pre-to-post-test, 13 reported a significant reduction; using the converted common metric we created, these reductions ranged from 0.20 to 3.33 points on a 10-point numeric rating scale.

Conclusions: AAI may be considered a promising approach in need of further, more rigorous research. Available evidence supporting AAI remains weak due to issues of study quality and design, thereby impeding our ability to draw reliable conclusions on the utility of AAI in relieving pain. Given the rapidly increasing availability of these interventions in hospitals, it is important to better understand its effectiveness.

Sullivan Mariah, Huberty Jennifer, Green Jeni, Cacciatore Joanne. Adding a Facebook Support Group to an Online Yoga Randomized Trial for Women Who Have Experienced Stillbirth: A Feasibility Study. *Journal of Integrative and Complementary Medicine 2022;*28(2): 179-87p.

Abstract:

Objectives: Women who experience stillbirth are more likely to develop post-traumatic stress disorder (PTSD), and anxious and depressive symptoms than those who deliver live healthy babies. Participants in a recent study of online yoga (OY) reported a desire for more social support, which may help reduce PTSD related to grief and aid in coping. Facebook (FB) has been used successfully to deliver support for online interventions, but little is known about its use in conjunction with OY. The purpose of this study was to examine the feasibility of a FB support group in conjunction with an 8-week OY intervention.

Design: Randomized parallel feasibility trial with a 1:1 study group allocation ratio.

Setting/Location: Online.

Subjects: Women (N = 60) who experienced stillbirth within the past 3 years.

Interventions: Participants were recruited nationally to participate and randomized into one of two groups: OY only (n = 30) or online yoga with Facebook (OYFB) (n = 30). Both groups were asked to complete 60 min of OY per week. Women in the OY group were asked to log on to a FB page at least once per week.

Outcome measures: Acceptability (i.e., satisfaction) and demand (i.e., attendance), PTSD, anxiety, depressive symptoms, social support.

Results: Participants were satisfied with and enjoyed OY, and 8/13 FB acceptability benchmarks were met. There were no significant differences between groups in minutes of yoga per week.

Conclusions: The addition of a FB group to an OY intervention for women who have experienced stillbirth is feasible, although more research is needed to increase its efficacy.

Suri M, Katnoria S, Walter NS, Manchanda RK, Khurana A, Nayak D et al. Efficacy of Chininum Sulphuricum 30C against Malaria: An in vitro and in vivo Study. *Complementary Medicine Research 2022;*29(1): 43-52p.

Abstract:

Background: New effective, economical and safe antimalarial drugs are urgently needed due to the development of multi-drug-resistant strains of the parasite. Homeopathy uses ultra-diluted doses of various substances to stimulate autoregulatory and self-healing processes to cure various ailments. The aim of the study was to evaluate the in vitro and in vivo antimalarial efficacy of a homeopathic drug, Chininum sulphuricum 30C.

Methods: In vitro antiplasmodial activity was screened against the P. falciparum chloroquine-sensitive (3D7) strain, and cell viability was assessed against normal human dermal fibroblasts and HepG2 cells. Suppressive, preventive and curative studies were carried out against P. berghei-infected mice in vivo.

Results: Chininum sulphuricum (30C) revealed good antiplasmodial activity in vitro, with 92.79 ± 6.93% inhibition against the 3D7 strain. The cell viability was 83.6 ± 0.6% against normal human dermal fibroblasts and 95.22 ± 5.1% against HepG2 cells. It also exhibited suppressive efficacy with 95.56% chemosuppression on day 7 with no mortality throughout the follow-up period of 28 days. It also showed preventive activity against the disease. Drug treatment was also safe to the liver and kidney function of the host as evidenced by biochemical studies.

Conclusion: Chininum sulphuricum 30C exhibited considerable antimalarial activity along with safety to the liver and kidney function of the host.

Talele Gitanjali, Vaidhya Shashikant, Chowdhary Abhay, Herscu Paul, Shah Rajesh. Randomized Double-Blind, Placebo-Controlled Feasibility Study, Evaluating the Efficacy of Homeopathic Medicines in the Prevention of COVID-19 in a Quarantined Population. *Homeopathy 2022;* 111(1): 49-56p.

Abstract:

Introduction: Exploring preventive therapeutic measures has been among the biggest challenges during the coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We explored the feasibility and methods of recruitment, retention, and potential signal of efficacy, of selected homeopathic medicines as preventive measure for developing COVID-19 in a multi-group study.

Methods: A six-group, randomized, double-blind, placebo-controlled prophylaxis study was conducted in a COVID-19 exposed population in a quarantine facility in Mumbai, India. Each group received one of the following: Arsenicum album 30c, Bryonia alba 30c, a combination (Arsenicum album 30c, Bryonia alba 30c, Gelsemium sempervirens 30c, and Influenzinum 30c), coronavirus nosode CVN01 30c, Camphora 1M, or placebo. Six pills twice a day were administered for 3 days. The primary outcome measure used was testing recruitment and retention in this quarantined setting. Secondary outcomes were numbers testing positive for COVID-19 after developing symptoms of illness, number of subjects hospitalized, and days to recovery.

Results: Good rates of recruitment and retention were achieved. Of 4,497 quarantined individuals, 2,343 sought enrollment, with 2,294 enrolled and 2,233 completing the trial (49.7% recruitment, 97.3% retention). Subjects who were randomized to either Bryonia alba or to the CVN01 nosode signaled ($p < 0.10$) a lower incidence of laboratory-confirmed COVID-19 and a shorter period of illness, with evidence of fewer hospitalizations, than those taking placebo. The three other groups did not show signals of efficacy.

Conclusion: This pilot study supports the feasibility of a larger randomized, double-blind, placebo-controlled trial. Bryonia alba 30c and CVN01 30c should both be explored in disease prevention or shortening the course of disease symptomatology in a COVID-19-exposed population.

Telke Susan, Leininger Brent, Hanson Linda, Kreitzer Mary Jo. Randomized Trial of 21 Days of Loving Kindness Meditation for Stress Reduction and Emotional Well-being Within an Online Health Community for Patients, Family, and Friends Experiencing a Cancer Health Journey. ***Journal of Integrative and Complementary Medicine 2022;*****28(2): 158-67p.**

Abstract:

Objectives: CaringBridge (CB) is an online health community for people undergoing challenging health journeys. Loving Kindness Meditation (LKM) is a systemized mind–body approach developed to increase loving acceptance and has previously been reported to increase resilience in the face of adversity.

Materials and Methods: Results of a randomized controlled trial of immediate compared with deferred 21-day LKM intervention in an online community are reported. The deferred group received LKM intervention after a waiting period of 3 weeks. Inclusion criteria were >18 years old, ability to understand English, willingness to participate in a mind–body practice, and use of CB for a cancer journey. Change in perceived stress, self-compassion, social connectedness and assurance, and compassionate love scales from baseline to 21 days was assessed.

Results: Of the 979 participants included in the study, 649 (66%) provided 3-week follow-up data and 330 (49%) self-reported engaging in the LKM practice 5 or more days/week. Participants in the immediate LKM group reported medium effect size improvement in stress (0.4), self-compassion (0.5), and social connectedness (0.4) compared with the deferred LKM group. Changes in perceived stress and self-compassion were larger in magnitude and increased with more frequent engagement in LKM.

Conclusions: The immediate LKM group showed improvements in stress, self-compassion, and social connectedness compared with the deferred control group. Differential study retention rates by treatment arm and self-reported engagement in LKM subject the results to selection bias. Future research of similar interventions within online health communities might pay greater attention to promoting intervention adherence and engaging a more diverse economic and racial/ethnic population.

Teut Michael, Haselen Robbert A van, Rutten Lex, Lamba Chetna Deep, Bleul Gerhard, Ulbrich Zurni Susanne. Case Reporting in Homeopathy—An Overview of Guidelines and Scientific Tools. ***Homeopathy 2022;*** **111(1): 2-9p.**

Abstract:

Case reports have been of central importance to the development of homeopathy over the past 200 years. With a special focus on homeopathy, we give an overview on guidelines and tools that may help to improve the quality of case reports. Reporting guidelines such as CARE (Case Report), HOM-CASE (Homeopathic Clinical Case Reports), and the WissHom Documentation Standard help to improve the quality of reporting and strengthen the scientific value of a case report. Additional scientific tools such as prospective outcome assessment, prognostic factor research, cognition-based medicine, and the Modified Naranjo Criteria for Homeopathy (MONARCH) score may be helpful in improving case documentation and evaluation.

Upadhyay Vikas, Saoji Apar Avinash, Verma Anita, Saxena Vartika. Development and validation of 20-min yoga module for reducing burnout among healthcare worker(s). ***Complementary Therapies in Clinical Practice 2022;*****46: Article 101543**

Abstract:

Background: A high prevalence of burnout has been reported among healthcare worker(s). During the current pandemic, such burnout has increased due to excessive load of patient care, use of personal protective equipment (PPE) kits, working in long shifts, staying away from family due to isolation norms, and disrupted social life. Existing yoga techniques used for reducing burnout include 45 min to hour-long sessions, which may not be feasible for regular practice by the healthcare worker(s).

Objective: The proposed study aimed to develop a 20-min yoga module to reduce burnout among healthcare worker(s).
Methods: To develop a 20-min yoga module, we reviewed yoga texts and relevant scientific research articles. Components of the 20-min yoga module include sukshma vyayama (loosening exercises), pranayama (regulated breathing), and dhyana (meditation). Nineteen yoga experts validated the 20-min yoga module with an average (SD) of 11.47 (6.77) years of research and clinical experience in yoga. Content validity ratio (CVR) was calculated according to Lawshe's method. Items having a CVR of 0.47 and above were retained in the module.

Results and conclusion: The content validity index (CVI) of the entire module was 0.83. CVR results of the elements of the 20-min yoga module indicated that experts consider these practices to be essential for reducing burnout among the healthcare worker(s). The strength of the 20-min yoga module lies in its short duration and easy-to-learn practices. 20-min yoga module can be implemented in practice by the healthcare worker(s) for reducing burnout following efficacy studies through further clinical trials.

Vahdat Mansoureh, Allahqoli Leila, Mirzaei Hossein, Giovannucci Edward, Alkatout Ibrahim. Effect of vitamin D on recurrence of uterine

fibroids: A randomized, double-blind, placebo-controlled pilot study. *Complementary Therapies in Clinical Practice 2022;*46: Article 101536

Abstract:

Background and purpose: A deficiency of vitamin D has been suggested as one of the principal risk factors for uterine fibroids (UFs). We aimed to investigate the effect of vitamin D supplementation on the recurrence of UFs.

Materials and methods: In a randomized, double-blind, placebo-controlled pilot study, women who had undergone hysteroscopic myomectomy from November 2017 to June 2020 were randomly given either vitamin D (1000 IU tablet; n = 55), or placebo (n = 54) daily for 12 months. Both groups were followed and compared in regard of the primary outcomes of the study, which were recurrence rates, size, and numbers of UFs based on three-dimensional transvaginal ultrasound investigation (3D-TVS). Data analysis was performed by the intention-to-treat (ITT) approach.

Results: The mean age of the study participants was 37.9 ± 6.5 years. The two groups did not differ significantly in terms of demographic and pre-intervention clinical characteristics. The administration of vitamin D supplements for one year reduced recurrence rates of UFs by 50% (p = 0.17). Vitamin D also reduced the size of recurrent UFs in the intervention group compared to controls (−7.7 mm), the difference was statistically different (p < 0.001). No adverse effect of vitamin D was reported in the present study.

Conclusion: Based on these results, vitamin D appears to be a promising and safe agent in the prevention of recurrence and reduction of the size of recurrent UFs, although further well-designed and appropriately powered studies are required to demonstrate a significant difference in the size and number of recurrent UFs.

Winser Stanley John, Pang Marco, Tsang William WN, Whitney Susan L. Tai Chi for Dynamic Balance Training Among Individuals with Cerebellar Ataxia: An Assessor-Blinded Randomized-Controlled Trial. *Journal of Integrative and Complementary Medicine 2022;*28(2): 146-57p.

Abstract:

Objective: To evaluate the immediate and long-term effects of 12 weeks of Tai Chi training on dynamic balance and disease severity among individuals with cerebellar ataxia (CA).

Design: An assessor-blinded, two-arm, parallel-group randomized-controlled trial was conducted among 24 participants with CA. Participants were randomized to receive either Tai Chi intervention (n = 12) or usual care (n = 12). Dynamic balance was assessed using the Berg Balance Scale (BBS),

Scale for the Assessment and Rating of Ataxia (SARA) balance sub-component of the SARA (SARAbal), Sensory Organization Test, and Limits of Stability test. Disease severity was assessed using the SARA and health-related quality of life using the EuroQol visual analog scale. Assessments were completed at baseline (week 0: T1), postintervention (week 12: T2), and at the end of the 24-week (week 36: T3) follow-up period.

Interventions: The 8-form Tai Chi exercise was delivered in 60-min sessions, three times a week for 12 weeks. Participants were asked to complete an unsupervised home Tai Chi exercise program over the next 24 weeks. Participants in the usual care control group completed all study measures but did not receive any intervention.

Results: Compared with the usual care control group, after 12 weeks of Tai Chi training, the experimental group demonstrated beneficial effects for dynamic balance assessed using the BBS (mean difference [MD]: 4, 95% confidence interval [CI]: −1.06 to 8.71) and the SARAbal (MD: −1.33, 95% CI: −2.66 to 2.33). The effect size ranged from small to large. The benefits gained were not sustained after 24 weeks during the follow-up assessment. Tai Chi did not benefit disease severity and health-related quality of life in this population.

Conclusion: Some evidence supports the immediate beneficial effects of 12 weeks of Tai Chi training on the dynamic balance among individuals with CA.

Wolverson E, Glover L, Clappison DJ. Self-Care for Family Carers: Can the Alexander Technique help? *Complementary Therapies in Clinical Practice 2022;*46: Article 101546

Abstract:

Background and purpose: Caring for a family member who is living with dementia can be incredibly challenging. Interventions to support family carers are vital and so carers should be supported to care for themselves and to maintain their own sense of self. The aim of this exploratory study was to explore the views of carers on the potential value of developing an Alexander Technique intervention for family carers of people with dementia.

Materials and methods: We delivered a one-off taster session of the Alexander Technique to family carers of people with dementia. Eight carers of people with dementia attended the group session led by two registered Alexander teachers. Post-session questionnaires examined carers' thoughts on the content, context, and process of learning the Alexander technique. A focus group at the end of the session asked participants to provide feedback on their experience and the perceived benefits for carers.

Results: Carers' satisfaction with the session was high and they reported benefitting from it. Participants appreciated having time for themselves in which they were able to stop to enjoy a moment of calm. They felt they could

use the ideas they gained from the session in everyday life. The use of touch in the sessions was also valued by carers.

Conclusion: This study provides preliminary evidence that the Alexander Technique has the potential to increase carers' ability to self-care and to support them in their caring. In so doing it has the potential to indirectly help those they care for.

Wu Na, Huang Rong, Shan Shanshan, Li Yuehong, Jiang Hui. Effect of the labour roadmap on anxiety, labour pain, sense of control, and gestational outcomes in primiparas. *Complementary Therapies in Clinical Practice 2022;*46: Article 101545

Abstract:

Background and purpose: The pain and uncertainty of the labour process can lead to anxiety. Birth ball exercises are one of the pain relief methods for the labour process. This study aimed to explore the outcomes of the use of the labour roadmap with birth balls in primiparas.

Materials and methods: This randomized controlled trial involved Chinese women between the gestational ages of 37–42 weeks who were randomly assigned to the experimental or control group. The outcomes of labour pain, anxiety, and self-control were collected using the Short-Form McGill Pain Questionnaire, visual analogue scale-anxiety, and Labor Agentry Scale, respectively.

Results: The study found improvements in anxiety, pain, and self-control ($P < 0.05$), as well as the duration of the first stage of labour ($P < 0.05$) in the intervention group, but there were no significant differences in the duration of the second and third stages of labour, volume of bleeding, or the 1-min Apgar score between the two groups ($P = 0.09$, 0.07, 0.06, 0.63, respectively).

Conclusion: The labour roadmap was effective for improving self-control, reducing pain and anxiety during labour, and accelerating the first stage of labour.

Wu Qiling, Zhao Jie, Guo Weili. Efficacy of massage therapy in improving outcomes in knee osteoarthritis: A systematic review and meta-analysis. *Complementary Therapies in Clinical Practice 2022;*46: Article 101522

Abstract:

Background and purpose: Massage therapy is being used for knee osteoarthritis. However, level-1 evidence is lacking. This systematic review and meta-analysis aimed to synthesize evidence on the effect of massage therapy on knee osteoarthritis.

Methods: PubMed, Embase, Ovid, Springer, and Google Scholar databases were searched up to May 8, 2021 for randomized controlled trials comparing massage with controls for knee osteoarthritis. Review manager was used for a random-effect meta-analysis. Risk of bias was assessed using the Cochrane collaboration risk assessment tool and certainty of evidence using Grading of Recommendations Assessment, Development, and Evaluation (GRADE).

Results: Twelve studies with 737 participants were included. After 1–4 weeks of therapy, there was a significant reduction in pain and stiffness scores in the massage group and after 6–8 weeks of therapy, there was a significant reduction in stiffness and functionality scores. There was no significant difference in outcomes with long-term therapy. A statistically significant reduction in stiffness scores was seen with aromatherapy massage. Aromatherapy massage was not superior to standard massage. The overall quality of evidence according to GRADE was low to moderate for standard massage therapy and very low for aromatherapy.

Conclusion: Massage therapy may lead to some improvement in pain, stiffness, and functionality scores in the short term but not in long term. Aromatherapy massage was not found to be any better than standard massage therapy. Current evidence is limited by methodological heterogeneity amongst trials and small sample size of the studies.

Yao Ziqian, Xu Zhongbo, Xu Tielong, Liu Xiaowu, Zhou Xu. Moxibustion for alleviating chemotherapy-induced gastrointestinal adverse effects: A systematic review of randomized controlled trials. *Complementary Therapies in Clinical Practice 2022;*46: Article 101527

Abstract:

Objective: This systematic review aims to assess whether moxibustion is effective and safe for gastrointestinal adverse effects, a common and thorny issue arising from chemotherapy.

Methods: Seven electronic databases were searched up to August 28, 2021, to identify randomized controlled trials (RCTs) comparing moxibustion versus non-moxibustion treatments for various gastrointestinal adverse effects after chemotherapy. The Karnofsky performance status (KPS) and quality of life scores and the incidence of moxibustion-related adverse events were also investigated. Effects in meta-analyses were measured by risk ratios (RRs) or mean differences (MDs).

Results: Thirty-two RCTs (n = 2990) were included. Compared to the controls, moxibustion significantly reduced the incidences of nausea/vomiting (RR 0.70, 95% CI 0.61–0.79), severe nausea/vomiting (RR 0.39, 95% CI 0.29–0.51), diarrhoea (RR 0.56, 95% CI 0.38–0.82), constipation (RR 0.59, 95% CI 0.44–0.78), and abdominal distension (RR 0.60, 95% CI 0.46–0.78). The KPS (MD 7.53, 95% CI 3.42–11.64) and quality of life (MD 8.88, 95% CI 0.96–16.80) scores were also significantly improved

after moxibustion. The results did not support a benefit of moxibustion on inappetence (RR 0.69, 95% CI 0.40–1.22) or abdominal pain (RR 0.60, 95% CI 0.28–1.30). All adverse events related to moxibustion were mild.

Conclusions: Moderate-to very-low-quality evidence suggests that moxibustion may be safely used as an adjuvant treatment after chemotherapy to reduce the incidences of nausea and vomiting, diarrhoea, constipation, and abdominal distension and improve the performance status and quality of life in patients with malignant tumours. Its effects on abdominal pain and inappetence are uncertain.

Ye Mingzhu, Zheng Yuhui, Xiong Zhenyu, Ye Bingzhao, Zheng Guohua. Baduanjin exercise ameliorates motor function in patients with post-stroke cognitive impairment: A randomized controlled trial. *Complementary Therapies in Clinical Practice 2022;*46: Article 101506

Abstract:

Background and purpose: As a traditional Chinese mind-body exercise, Baduanjin has been documented to have a positive effect on cognitive and physical function in a wide range of populations, but it is unclear whether it helps improve motor function in patients with post-stroke cognitive impairment (PSCI). The aim of this two-arm, randomized, parallel controlled study was to explore the rehabilitation effect of Baduanjin exercise on motor function in patients with PSCI.

Materials and methods: Forty-eight patients with PSCI were randomly assigned to control and intervention groups. The control group received health education sessions on stroke prevention and rehabilitation. The intervention group received Baduanjin training in addition to the health education intervention. Before and after the 24-week intervention, both groups completed the Fugl-Meyer Assessment (FMA), Berg Balance Scale (BBS), Manual Muscle Test (MMT), Modified Ashworth Scale (MAS), and Three-Dimensional Gait Analysis (3DGA).

Results: After the 24-week intervention, both groups showed significant improvements in the FMA, BBS, MMT and MAS test results, but the Baduanjin group exhibited significantly better FMA, BBS and MMT test results than the control group (all $P < 0.05$). Furthermore, the Baduanjin exercise group showed significant improvements in spatial gait parameters, including the step length, walking speed and cadence, which were significantly better than the control group (all $P < 0.05$). No adverse events were reported during the study period.

Conclusion: The 24-week Baduanjin exercise training may improve the limb motor function, balance, muscle strength and gait function of individuals with PSCI.

Zafereo Jason, Jones Stephanie, Jarrett Robin B, Frost Samantha, Noe Carl. Improved symptoms of complex regional pain syndrome after novel lymphatic treatment and interdisciplinary pain management. *Complementary Therapies in Clinical Practice 2022;*46: Article 101512

Abstract:

Introduction: Complex regional pain syndrome (CRPS) is a pain syndrome with no singular mechanism and no specific cure. The aim of this case report is to study the impact of Lymphatic Enhancement Technology (LET) treatment on CRPS-related symptoms.

Methods: A 51 year-old female presented with a chief complaint of severe, refractory ankle pain and CRPS related to a tibial and fibular fracture sustained three years earlier. The patient completed twelve cognitive behavioral therapy sessions over a 4-week period, and eleven physical therapy sessions over a four-month period, six of which utilized LET.

Results: Pain and swelling were largely unchanged with interdisciplinary treatment before the introduction of LET. A within-session change of 37.5% in pain intensity and 87.5% in ankle girth was observed immediately after the first application of LET. Three months after beginning LET treatment, the patient maintained a 43.8% improvement in pain intensity and 100% improvement in measurements of lower extremity girth and ankle range of motion. No side effects or adverse events were associated with the LET treatment.

Conclusion: Swelling, pain, and mobility loss are common symptoms and features of CRPS. LET is a novel, non-invasive treatment that appears to be quite safe and effective for improving pain, swelling, and mobility loss related to CRPS.

Zhou Xue, Li Xiuling, Ding Hui, Lu Ying. Acupuncture effects on in-vitro fertilization pregnancy outcomes: A meta-analysis. *Complementary Therapies in Clinical Practice 2022;*46: Article 101525

Abstract:

Background: The effects of acupuncture on in-vitro fertilization outcomes remain controversial. This study aimed to perform a meta-analysis to assess the effectiveness of acupuncture as an adjuvant therapy to embryo transfer compared to sham-controls or no adjuvant therapy controls on improving pregnancy outcomes in women undergoing in-vitro fertilization.

Methods: A systematic literature search up to January 2021 was performed and 29 studies included 6623 individuals undergoing in-vitro fertilization at the baseline of the study; 3091 of them were using acupuncture as an adjuvant therapy to embryo transfer, 1559 of them were using sham-

controls, and 1441 of them were using no adjuvant therapy controls. They reported a comparison between the effectiveness of acupuncture as an adjuvant therapy to embryo transfer compared to sham-controls or no adjuvant therapy controls on improving pregnancy outcomes in women undergoing in-vitro fertilization. Odds ratio (OR) with 95% confidence intervals (CIs) were calculated assessing the effectiveness of acupuncture as an adjuvant therapy to embryo transfer compared to sham-controls or no adjuvant therapy controls using the dichotomous method with a random or fixed-effect model.

Results: Significantly higher outcomes with acupuncture were observed in biochemical pregnancy (OR, 1.98; 95% CI, 1.55–2.53, $p < 0.001$); clinical pregnancy (OR, 1.70; 95% CI, 1.46–1.98, $p < 0.001$); ongoing pregnancy (OR, 1.78; 95% CI, 1.41–2.26, $p < 0.001$); and live birth (OR, 1.58; 95% CI, 1.15–2.18, $p = 0.005$) compared to no adjuvant therapy controls. However, no significant difference were found between acupuncture and no adjuvant therapy controls in miscarriage (OR, 0.96; 95% CI, 0.48–1.92, $p = 0.91$).

No significant difference was observed with acupuncture in biochemical pregnancy (OR, 1.16; 95% CI, 0.65–2.08, $p = 0.62$); clinical pregnancy (OR, 1.13; 95% CI, 0.83–1.54, $p = 0.43$); ongoing pregnancy (OR, 1.04; 95% CI, 0.66–1.62, $p = 0.87$); live birth (OR, 1.02; 95% CI, 0.73–1.42, $p = 0.90$), and miscarriage (OR, 1.16; 95% CI, 0.86–1.55, $p = 0.34$) compared to sham-controls.

Conclusions: Using acupuncture as an adjuvant therapy to embryo transfer may improve the biochemical pregnancy, clinical pregnancy, ongoing pregnancy, and live birth outcomes compared to no adjuvant therapy controls. However, no significant difference was found between acupuncture as an adjuvant therapy to embryo transfer and sham-controls in any of the measured outcomes. This relationship forces us to recommend the use of acupuncture as adjuvant therapy in women undergoing in-vitro fertilization and inquire further studies comparing acupuncture and sham-controls to reach the best procedure.

Allied System of Medicine

Boden William E, Kaski Juan Carlos, Al-Lamee Rasha, Weintraub William S. What constitutes an appropriate empirical trial of antianginal therapy in patients with stable angina before referral for revascularisation? *Lancet 2022;*399(10325): 691-94p.

Burki Talha. Research Focus: The Arc Institute. *Lancet 2022;*399(10326): 708p.

Casirivimab and imdevimab in patients admitted to hospital with COVID-19 (RECOVERY): A randomised, controlled, open-label, platform trial. *Lancet 2022;*399(10325): 665-76p.

Abstract:

Background: Casirivimab and imdevimab are non-competing monoclonal antibodies that bind to two different sites on the receptor binding domain of the SARS-CoV-2 spike glycoprotein, blocking viral entry into host cells. We aimed to evaluate the efficacy and safety of casirivimab and imdevimab administered in combination in patients admitted to hospital with COVID-19.

Methods: RECOVERY is a randomised, controlled, open-label platform trial comparing several possible treatments with usual care in patients admitted to hospital with COVID-19. 127 UK hospitals took part in the evaluation of casirivimab and imdevimab. Eligible participants were any patients aged at least 12 years admitted to hospital with clinically suspected or laboratory-confirmed SARS-CoV-2 infection. Participants were randomly assigned (1:1) to either usual standard of care alone or usual care plus casirivimab 4 g and imdevimab 4 g administered together in a single intravenous infusion. Investigators and data assessors were masked to analyses of the outcome data during the trial. The primary outcome was 28-day all-cause mortality assessed by intention to treat, first only in patients without detectable antibodies to SARS-CoV-2 infection at randomisation (ie, those who were seronegative) and then in the overall population. Safety was assessed in all participants who received casirivimab and imdevimab. The trial is registered with ISRCTN (50189673) and ClinicalTrials.gov (NCT04381936).

Findings: Between Sept 18, 2020, and May 22, 2021, 9785 patients enrolled in RECOVERY were eligible for casirivimab and imdevimab, of

which 4839 were randomly assigned to casirivimab and imdevimab plus usual care and 4946 to usual care alone. 3153 (32%) of 9785 patients were seronegative, 5272 (54%) were seropositive, and 1360 (14%) had unknown baseline antibody status. 812 (8%) patients were known to have received at least one dose of a SARS-CoV-2 vaccine. In the primary efficacy population of seronegative patients, 396 (24%) of 1633 patients allocated to casirivimab and imdevimab versus 452 (30%) of 1520 patients allocated to usual care died within 28 days (rate ratio [RR] 0·79, 95% CI 0·69–0·91; p=0·0009). In an analysis of all randomly assigned patients (regardless of baseline antibody status), 943 (19%) of 4839 patients allocated to casirivimab and imdevimab versus 1029 (21%) of 4946 patients allocated to usual care died within 28 days (RR 0·94, 95% CI 0·86–1·02; p=0·14). The proportional effect of casirivimab and imdevimab on mortality differed significantly between seropositive and seronegative patients (p value for heterogeneity=0·002). There were no deaths attributed to the treatment, or meaningful between-group differences in the pre-specified safety outcomes of cause-specific mortality, cardiac arrhythmia, thrombosis, or major bleeding events. Serious adverse reactions reported in seven (<1%) participants were believed by the local investigator to be related to treatment with casirivimab and imdevimab.

Interpretation: In patients admitted to hospital with COVID-19, the monoclonal antibody combination of casirivimab and imdevimab reduced 28-day mortality in patients who were seronegative (and therefore had not mounted their own humoral immune response) at baseline but not in those who were seropositive at baseline.

Funding: UK Research and Innovation (Medical Research Council) and National Institute of Health Research.

Cerdeira Ana Sofia, Ismail Lamiese, Moore Niall, George Bruce, Majd Hooman Soleymani. Retroperitoneal leiomyomatosis: A benign outcome of power morcellation with potentially serious consequences. ***Lancet 2022;*****399(10324): 554p.**

Clemens Sue Ann Costa, Weckx Lily, Clemens Ralf, Mendes Ana Verena Almeida, Matos Laiana Januse de Arruda Cordeiro. Heterologous versus homologous COVID-19 booster vaccination in previous recipients of two doses of CoronaVac COVID-19 vaccine in Brazil (RHH-001): A phase 4, non-inferiority, single blind, randomised study. ***Lancet 2022;*****399(10324): 521-29p.**

Abstract:

Introduction: The inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac, Sinovac) has been widely used in a two-dose schedule. We assessed whether a third dose of the homologous or a different vaccine could boost immune responses.

Methods: RHH-001 is a phase 4, participant masked, two centre, safety and immunogenicity study of Brazilian adults (18 years and older) in São Paulo or Salvador who had received two doses of CoronaVac 6 months previously. The third heterologous dose was of either a recombinant adenoviral vectored vaccine (Ad26.COV2-S, Janssen), an mRNA vaccine (BNT162b2, Pfizer–BioNTech), or a recombinant adenoviral-vectored ChAdOx1 nCoV-19 vaccine (AZD1222, AstraZeneca), compared with a third homologous dose of CoronaVac. Participants were randomly assigned (5:6:5:5) by a RedCAP computer randomisation system stratified by site, age group (18–60 years or 61 years and over), and day of randomisation, with a block size of 42. The primary outcome was non-inferiority of anti-spike IgG antibodies 28 days after the booster dose in the heterologous boost groups compared with homologous regimen, using a non-inferiority margin for the geometric mean ratio (heterologous vs homologous) of 0·67. Secondary outcomes included neutralising antibody titres at day 28, local and systemic reactogenicity profiles, adverse events, and serious adverse events. This study was registered with Registro Brasileiro de Ensaios Clínicos, number RBR–9nn3scw.

Findings: Between Aug 16, and Sept 1, 2021, 1240 participants were randomly assigned to one of the four groups, of whom 1239 were vaccinated and 1205 were eligible for inclusion in the primary analysis. Antibody concentrations were low before administration of a booster dose with detectable neutralising antibodies of 20·4% (95% CI 12·8–30·1) in adults aged 18–60 years and 8·9% (4·2–16·2) in adults 61 years or older. From baseline to day 28 after the booster vaccine, all groups had a substantial rise in IgG antibody concentrations: the geometric fold-rise was 77 (95% CI 67–88) for Ad26.COV2-S, 152 (134–173) for BNT162b2, 90 (77–104) for ChAdOx1 nCoV-19, and 12 (11–14) for CoronaVac. All heterologous regimens had anti-spike IgG responses at day 28 that were superior to homologous booster responses: geometric mean ratios (heterologous vs homologous) were 6·7 (95% CI 5·8–7·7) for Ad26.COV2-S, 13·4 (11·6–15·3) for BNT162b2, and 7·0 (6·1–8·1) for ChAdOx1 nCoV-19. All heterologous boost regimens induced high concentrations of pseudovirus neutralising antibodies. At day 28, all groups except for the homologous boost in the older adults reached 100% seropositivity: geometric mean ratios (heterologous vs homologous) were 8·7 (95% CI 5·9–12·9) for Ad26.COV2-S vaccine, 21·5 (14·5–31·9) for BNT162b2, and 10·6 (7·2–15·6)

for ChAdOx1 nCoV-19. Live virus neutralising antibodies were also boosted against delta (B.1.617.2) and omicron variants (B.1.1.529). There were five serious adverse events. Three of which were considered possibly related to the vaccine received: one in the BNT162b2 group and two in the Ad26.COV2-S group. All participants recovered and were discharged home.

Interpretation: Antibody concentrations were low at 6 months after previous immunisation with two doses of CoronaVac. However, all four vaccines administered as a third dose induced a significant increase in binding and neutralising antibodies, which could improve protection against infection. Heterologous boosting resulted in more robust immune responses than homologous boosting and might enhance protection.

Funding: Ministry of Health, Brazil.

Gershenson David M, Miller Austin, Brady William E, Paul James, Gourley Charlie. Trametinib versus standard of care in patients with recurrent low-grade serous ovarian cancer (GOG 281/LOGS): An international, randomised, open-label, multicentre, phase 2/3 trial. *Lancet 2022;*399(10324): 541-53p.

Abstract:

Background: Low-grade serous carcinoma of the ovary or peritoneum is characterised by MAPK pathway aberrations and its reduced sensitivity to chemotherapy relative to high-grade serous carcinoma. We compared the MEK inhibitor trametinib to physician's choice standard of care in patients with recurrent low-grade serous carcinoma.

Methods: This international, randomised, open-label, multicentre, phase 2/3 trial was done at 84 hospitals in the USA and UK. Eligible patients were aged 18 years or older with recurrent low-grade serous carcinoma and measurable disease, as defined by Response Evaluation Criteria In Solid Tumors version 1.1, had received at least one platinum-based regimen, but not all five standard-of-care drugs, and had received an unlimited number of previous regimens. Patients with serous borderline tumours or tumours containing low-grade serous and high-grade serous carcinoma were excluded. Eligible patients were randomly assigned (1:1) to receive either oral trametinib 2 mg once daily (trametinib group) or one of five standard-of-care treatment options (standard-of-care group): intravenous paclitaxel 80 mg/m2 by body surface area on days 1, 8, and 15 of every 28-day cycle; intravenous pegylated liposomal doxorubicin 40–50 mg/m2 by body surface area once every 4 weeks; intravenous topotecan 4 mg/m2 by body

surface area on days 1, 8, and 15 of every 28-day cycle; oral letrozole 2·5 mg once daily; or oral tamoxifen 20 mg twice daily. Randomisation was stratified by geographical region (USA or UK), number of previous regimens (1, 2, or ≥3), performance status (0 or 1), and planned standard-of-care regimen. The primary endpoint was investigator-assessed progression-free survival while receiving randomised therapy, as assessed by imaging at baseline, once every 8 weeks for 15 months, and then once every 3 months thereafter, in the intention-to-treat population. Safety was assessed in patients who received at least one dose of study therapy. This trial is registered with ClinicalTrials.gov, NCT02101788, and is active but not recruiting.

Findings: Between Feb 27, 2014, and April 10, 2018, 260 patients were enrolled and randomly assigned to the trametinib group (n=130) or the standard-of-care group (n=130). At the primary analysis, there were 217 progression-free survival events (101 [78%] in the trametinib group and 116 [89%] in the standard-of-care group). Median progression-free survival in the trametinib group was 13·0 months (95% CI 9·9–15·0) compared with 7·2 months (5·6–9·9) in the standard-of-care group (hazard ratio 0·48 [95% CI 0·36–0·64]; p<0·0001). The most frequent grade 3 or 4 adverse events in the trametinib group were skin rash (17 [13%] of 128), anaemia (16 [13%]), hypertension (15 [12%]), diarrhoea (13 [10%]), nausea (12 [9%]), and fatigue (ten [8%]). The most frequent grade 3 or 4 adverse events in the standard-of-care group were abdominal pain (22 [17%]), nausea (14 [11%]), anaemia (12 [10%]), and vomiting (ten [8%]). There were no treatment-related deaths.

Interpretation: Trametinib represents a new standard-of-care option for patients with recurrent low-grade serous carcinoma.

Funding: NRG Oncology, Cancer Research UK, Target Ovarian Cancer, and Novartis.

Health and health care in Ukraine: in transition and at risk. *Lancet 2022;*399(10325): 605p.

Heier Jeffrey S, Khanani Arshad M, Ruiz Carlos Quezada, Basu Karen, Zeolite Carlos. Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): Two randomised, double-masked, phase 3, non-inferiority trials. *Lancet 2022;*399(10326): 729-40p.

Abstract:

Background: Faricimab is a bispecific antibody that acts through dual inhibition of both angiopoietin-2 and vascular endothelial growth factor A. We report primary results of two phase 3 trials evaluating intravitreal faricimab with extension up to every 16 weeks for neovascular age-related macular degeneration (nAMD).

Methods: TENAYA and LUCERNE were randomised, double-masked, non-inferiority trials across 271 sites worldwide. Treatment-naive patients with nAMD aged 50 years or older were randomly assigned (1:1) to intravitreal faricimab 6·0 mg up to every 16 weeks, based on protocol-defined disease activity assessments at weeks 20 and 24, or aflibercept 2·0 mg every 8 weeks. Randomisation was performed through an interactive voice or web-based response system using a stratified permuted block randomisation method. Patients, investigators, those assessing outcomes, and the funder were masked to group assignments. The primary endpoint was mean change in best-corrected visual acuity (BCVA) from baseline averaged over weeks 40, 44, and 48 (prespecified non-inferiority margin of four letters), in the intention-to-treat population. Safety analyses included patients who received at least one dose of study treatment. These trials are registered with ClinicalTrials.gov (TENAYA NCT03823287 and LUCERNE NCT03823300).

Findings: Across the two trials, 1329 patients were randomly assigned between Feb 19 and Nov 19, 2019 (TENAYA n=334 faricimab and n=337 aflibercept), and between March 11 and Nov 1, 2019 (LUCERNE n=331 faricimab and n=327 aflibercept). BCVA change from baseline with faricimab was non-inferior to aflibercept in both TENAYA (adjusted mean change 5·8 letters [95% CI 4·6 to 7·1] and 5·1 letters [3·9 to 6·4]; treatment difference 0·7 letters [−1·1 to 2·5]) and LUCERNE (6·6 letters [5·3 to 7·8] and 6·6 letters [5·3 to 7·8]; treatment difference 0·0 letters [–1·7 to 1·8]). Rates of ocular adverse events were comparable between faricimab and aflibercept (TENAYA n=121 [36·3%] vs n=128 [38·1%], and LUCERNE n=133 [40·2%] vs n=118 [36·2%]).

Interpretation: Visual benefits with faricimab given at up to 16-week intervals demonstrates its potential to meaningfully extend the time between treatments with sustained efficacy, thereby reducing treatment burden in patients with nAMD.

Funding: F Hoffmann-La Roche.

Hubschen Judith M, Gouandjika Vasilache Ionela, Dina Julia. Measles. *Lancet 2022;*399(10325): 678-90p.

Abstract:

Measles is a highly contagious, potentially fatal, but vaccine-preventable disease caused by measles virus. Symptoms include fever, maculopapular rash, and at least one of cough, coryza, or conjunctivitis, although vaccinated individuals can have milder or even no symptoms. Laboratory diagnosis relies largely on the detection of specific IgM antibodies in serum, dried blood spots, or oral fluid, or the detection of viral RNA in throat or nasopharyngeal swabs, urine, or oral fluid. Complications can affect many organs and often include otitis media, laryngotracheobronchitis, pneumonia, stomatitis, and diarrhoea. Neurological complications are uncommon but serious, and can occur during or soon after the acute disease (eg, acute disseminated encephalomyelitis) or months or even years later (eg, measles inclusion body encephalitis and subacute sclerosing panencephalitis). Patient management mainly involves supportive therapy, such as vitamin A supplementation, monitoring for and treatment of secondary bacterial infections with antibiotics, and rehydration in the case of severe diarrhoea. There is no specific antiviral therapy for the treatment of measles, and disease control largely depends on prevention. However, despite the availability of a safe and effective vaccine, measles is still endemic in many countries and causes considerable morbidity and mortality, especially among children in resource-poor settings. The low case numbers reported in 2020, after a worldwide resurgence of measles between 2017 and 2019, have to be interpreted cautiously, owing to the effect of the COVID-19 pandemic on disease surveillance. Disrupted vaccination activities during the pandemic increase the potential for another resurgence of measles in the near future, and effective, timely catch-up vaccination campaigns, strong commitment and leadership, and sufficient resources will be required to mitigate this threat.

Humphreys Keith, Shover Chelsea L, Andrews Christina M, Bohnert Amy S B, Timko Christine. Responding to the opioid crisis in North America and beyond: recommendations of the Stanford–Lancet Commission. *Lancet 2022;*399(10324): 555-604p.

Makoni Munyaradzi. Burkina Faso crisis hits health care. *Lancet 2022;*399(10325): 616p.

Managing the opioid crisis in North America and beyond. *Lancet 2022;*399(10324): 495p.

Murray Christopher JL, Ikuta Kevin Shunji, Sharara Fablina, Swetschinski Lucien, Naghavi Mohsen. Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *Lancet 2022;*399(10325): 629-55p.

Abstract:

Background: Antimicrobial resistance (AMR) poses a major threat to human health around the world. Previous publications have estimated the effect of AMR on incidence, deaths, hospital length of stay, and health-care costs for specific pathogen–drug combinations in select locations. To our knowledge, this study presents the most comprehensive estimates of AMR burden to date.

Methods: We estimated deaths and disability-adjusted life-years (DALYs) attributable to and associated with bacterial AMR for 23 pathogens and 88 pathogen–drug combinations in 204 countries and territories in 2019. We obtained data from systematic literature reviews, hospital systems, surveillance systems, and other sources, covering 471 million individual records or isolates and 7585 study-location-years. We used predictive statistical modelling to produce estimates of AMR burden for all locations, including for locations with no data. Our approach can be divided into five broad components: number of deaths where infection played a role, proportion of infectious deaths attributable to a given infectious syndrome, proportion of infectious syndrome deaths attributable to a given pathogen, the percentage of a given pathogen resistant to an antibiotic of interest, and the excess risk of death or duration of an infection associated with this resistance. Using these components, we estimated disease burden based on two counterfactuals: deaths attributable to AMR (based on an alternative scenario in which all drug-resistant infections were replaced by drug-susceptible infections), and deaths associated with AMR (based on an alternative scenario in which all drug-resistant infections were replaced by no infection). We generated 95% uncertainty intervals (UIs) for final estimates as the 25th and 975th ordered values across 1000 posterior draws, and models were cross-validated for out-of-sample predictive validity. We present final estimates aggregated to the global and regional level.

Findings: On the basis of our predictive statistical models, there were an estimated 4·95 million (3·62–6·57) deaths associated with bacterial AMR in 2019, including 1·27 million (95% UI 0·911–1·71) deaths attributable to bacterial AMR. At the regional level, we estimated the all-age death rate attributable to resistance to be highest in western sub-Saharan Africa, at

27·3 deaths per 100 000 (20·9–35·3), and lowest in Australasia, at 6·5 deaths (4·3–9·4) per 100 000. Lower respiratory infections accounted for more than 1·5 million deaths associated with resistance in 2019, making it the most burdensome infectious syndrome. The six leading pathogens for deaths associated with resistance (Escherichia coli, followed by Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa) were responsible for 929 000 (660 000–1 270 000) deaths attributable to AMR and 3·57 million (2·62–4·78) deaths associated with AMR in 2019. One pathogen–drug combination, meticillin-resistant S aureus, caused more than 100 000 deaths attributable to AMR in 2019, while six more each caused 50 000–100 000 deaths: multidrug-resistant excluding extensively drug-resistant tuberculosis, third-generation cephalosporin-resistant E coli, carbapenem-resistant A baumannii, fluoroquinolone-resistant E coli, carbapenem-resistant K pneumoniae, and third-generation cephalosporin-resistant K pneumoniae.

Interpretation: To our knowledge, this study provides the first comprehensive assessment of the global burden of AMR, as well as an evaluation of the availability of data. AMR is a leading cause of death around the world, with the highest burdens in low-resource settings. Understanding the burden of AMR and the leading pathogen–drug combinations contributing to it is crucial to making informed and location-specific policy decisions, particularly about infection prevention and control programmes, access to essential antibiotics, and research and development of new vaccines and antibiotics. There are serious data gaps in many low-income settings, emphasising the need to expand microbiology laboratory capacity and data collection systems to improve our understanding of this important human health threat.

Funding: Bill & Melinda Gates Foundation, Wellcome Trust, and Department of Health and Social Care using UK aid funding managed by the Fleming Fund.

Nordstrom Peter, Ballin Marcel, Nordstrom Anna. Risk of infection, hospitalisation, and death up to 9 months after a second dose of COVID-19 vaccine: A retrospective, total population cohort study in Sweden. *Lancet 2022;*399(10327): 814-23p.

Abstract:

Background: Vaccine effectiveness against COVID-19 beyond 6 months remains incompletely understood. We aimed to investigate the effectiveness

of COVID-19 vaccination against the risk of infection, hospitalisation, and death during the first 9 months after vaccination for the total population of Sweden.

Methods: This retrospective, total population cohort study was done using data from Swedish nationwide registers. The cohort comprised all individuals vaccinated with two doses of ChAdOx1 nCoV-19, mRNA-1273, or BNT162b2, and matched unvaccinated individuals, with data on vaccinations and infections updated until Oct 4, 2021. Two outcomes were evaluated. The first was SARS-CoV-2 infection of any severity from Jan 12 to Oct 4, 2021. The second was severe COVID-19, defined as hospitalisation for COVID-19 or all-cause 30-day mortality after confirmed infection, from March 15 to Sept 28, 2021.

Findings: Between Dec 28, 2020, and Oct 4, 2021, 842 974 individuals were fully vaccinated (two doses), and were matched (1:1) to an equal number of unvaccinated individuals (total study cohort n=1 685 948). For the outcome SARS-CoV-2 infection of any severity, the vaccine effectiveness of BNT162b2 waned progressively over time, from 92% (95% CI 92 to 93; p<0·001) at 15–30 days, to 47% (39 to 55; p<0·001) at 121–180 days, and to 23% (−2 to 41; p=0·07) from day 211 onwards. Waning was slightly slower for mRNA-1273, with a vaccine effectiveness of 96% (94 to 97; p<0·001) at 15–30 days and 59% (18 to 79; p=0·012) from day 181 onwards. Waning was also slightly slower for heterologous ChAdOx1 nCoV-19 plus an mRNA vaccine, for which vaccine effectiveness was 89% (79 to 94; p<0·001) at 15–30 days and 66% (41 to 80; p<0·001) from day 121 onwards. By contrast, vaccine effectiveness for homologous ChAdOx1 nCoV-19 vaccine was 68% (52 to 79; p<0·001) at 15–30 days, with no detectable effectiveness from day 121 onwards (−19% [–98 to 28]; p=0·49). For the outcome of severe COVID-19, vaccine effectiveness waned from 89% (82 to 93; p<0·001) at 15–30 days to 64% (44 to 77; p<0·001) from day 121 onwards. Overall, there was some evidence for lower vaccine effectiveness in men than in women and in older individuals than in younger individuals.

Interpretation: We found progressively waning vaccine effectiveness against SARS-CoV-2 infection of any severity across all subgroups, but the rate of waning differed according to vaccine type. With respect to severe COVID-19, vaccine effectiveness seemed to be better maintained, although some waning became evident after 4 months. The results strengthen the evidence-based rationale for administration of a third vaccine dose as a booster.

Funding: None.

Our commitment to help accelerate progress against cancer. *Lancet 2022;*399(10327): 769p.

Pashankar Rashmi, Prabulos Anne Marie, Feder Henry M. Woman pregnant with twins has fever, haemolysis, and thrombocytopenia caused by babesiosis: could be confused with HELLP syndrome. *Lancet 2022;*399(10327): e10

Peeling Rosanna W, Heymann David L, Teo Yik Ying, Garcia Patricia J. Diagnostics for COVID-19: Moving from pandemic response to control. *Lancet 2022;*399(10326): 757-68p.

Abstract:

Diagnostics have proven to be crucial to the COVID-19 pandemic response. There are three major methods for the detection of SARS-CoV-2 infection and their role has evolved during the course of the pandemic. Molecular tests such as PCR are highly sensitive and specific at detecting viral RNA, and are recommended by WHO for confirming diagnosis in individuals who are symptomatic and for activating public health measures. Antigen rapid detection tests detect viral proteins and, although they are less sensitive than molecular tests, have the advantages of being easier to do, giving a faster time to result, of being lower cost, and able to detect infection in those who are most likely to be at risk of transmitting the virus to others. Antigen rapid detection tests can be used as a public health tool for screening individuals at enhanced risk of infection, to protect people who are clinically vulnerable, to ensure safe travel and the resumption of schooling and social activities, and to enable economic recovery. With vaccine roll-out, antibody tests (which detect the host's response to infection or vaccination) can be useful surveillance tools to inform public policy, but should not be used to provide proof of immunity, as the correlates of protection remain unclear. All three types of COVID-19 test continue to have a crucial role in the transition from pandemic response to pandemic control.

Pogson Jacob M, Halmagyi G Michael. Hearing but not understanding: word deafness from a brainstem lesion. *Lancet 2022;*399(10326): 756p.

Polizzotto Mark N, Nordwall Jacqueline, Babiker Abdel G, Phillips Andrew, Lane H Clifford. Hyperimmune immunoglobulin for hospitalised patients with COVID-19 (ITAC): A double-blind, placebo-

controlled, phase 3, randomised trial. *Lancet 2022;*399(10324): 530-40p.

Abstract:

Background: Passive immunotherapy using hyperimmune intravenous immunoglobulin (hIVIG) to SARS-CoV-2, derived from recovered donors, is a potential rapidly available, specific therapy for an outbreak infection such as SARS-CoV-2. Findings from randomised clinical trials of hIVIG for the treatment of COVID-19 are limited.

Methods: In this international randomised, double-blind, placebo-controlled trial, hospitalised patients with COVID-19 who had been symptomatic for up to 12 days and did not have acute end-organ failure were randomly assigned (1:1) to receive either hIVIG or an equivalent volume of saline as placebo, in addition to remdesivir, when not contraindicated, and other standard clinical care. Randomisation was stratified by site pharmacy; schedules were prepared using a mass-weighted urn design. Infusions were prepared and masked by trial pharmacists; all other investigators, research staff, and trial participants were masked to group allocation. Follow-up was for 28 days. The primary outcome was measured at day 7 by a seven-category ordinal endpoint that considered pulmonary status and extrapulmonary complications and ranged from no limiting symptoms to death. Deaths and adverse events, including organ failure and serious infections, were used to define composite safety outcomes at days 7 and 28. Prespecified subgroup analyses were carried out for efficacy and safety outcomes by duration of symptoms, the presence of anti-spike neutralising antibodies, and other baseline factors. Analyses were done on a modified intention-to-treat (mITT) population, which included all randomly assigned participants who met eligibility criteria and received all or part of the assigned study product infusion. This study is registered with ClinicalTrials.gov, NCT04546581.

Findings: From Oct 8, 2020, to Feb 10, 2021, 593 participants (n=301 hIVIG, n=292 placebo) were enrolled at 63 sites in 11 countries; 579 patients were included in the mITT analysis. Compared with placebo, the hIVIG group did not have significantly greater odds of a more favourable outcome at day 7; the adjusted OR was 1·06 (95% CI 0·77–1·45; p=0·72). Infusions were well tolerated, although infusion reactions were more common in the hIVIG group (18·6% vs 9·5% for placebo; p=0·002). The percentage with the composite safety outcome at day 7 was similar for the hIVIG (24%) and placebo groups (25%; OR 0·98, 95% CI 0·66–1·46; p=0·91). The ORs for the day 7 ordinal outcome did not vary for subgroups

considered, but there was evidence of heterogeneity of the treatment effect for the day 7 composite safety outcome: risk was greater for hIVIG compared with placebo for patients who were antibody positive (OR 2·21, 95% CI 1·14–4·29); for patients who were antibody negative, the OR was 0·51 (0·29–0·90; pinteraction=0·001).

Interpretation: When administered with standard of care including remdesivir, SARS-CoV-2 hIVIG did not demonstrate efficacy among patients hospitalised with COVID-19 without end-organ failure. The safety of hIVIG might vary by the presence of endogenous neutralising antibodies at entry.

Funding: US National Institutes of Health.

Power and bullying in research. *Lancet 2022;*399(10326): 695p.

Schneider Thoma Johannes, Chalkou Konstantina, Dorries Carola, Bighelli Irene, Leucht Stefan. Comparative efficacy and tolerability of 32 oral and long-acting injectable antipsychotics for the maintenance treatment of adults with schizophrenia: A systematic review and network meta-analysis. *Lancet 2022;*399(10327): 824-36p.

Abstract:

Background: Schizophrenia is a common, severe, and usually chronic disorder. Maintenance treatment with antipsychotic drugs can prevent relapse but also causes side-effects. We aimed to compare the efficacy and tolerability of antipsychotics as maintenance treatment for non-treatment resistant patients with schizophrenia.

Methods: In this systematic review and network meta-analysis, we searched, without language restrictions, the Cochrane Schizophrenia Group's specialised register between database inception and April 27, 2020, PubMed from April 1, 2020, to Jan 15, 2021, and the lists of included studies from related systematic reviews. We included randomised controlled trials (RCTs; ≥12 weeks of follow-up) that recruited adult participants with schizophrenia or schizoaffective disorder with stable symptoms who were treated with antipsychotics (monotherapy; oral or long-acting injectable) or placebo. We excluded RCTs of participants with specific comorbidities or treatment resistance. In duplicate, two authors independently selected eligible RCTs and extracted aggregate data. The primary outcome was the number of participants who relapsed and was

analysed by random-effects, Bayesian network meta-analyses. The study was registered on PROSPERO, CRD42016049022.

Findings: We identified 4157 references through our search, from which 501 references on 127 RCTs of 32 antipsychotics (comprising 18 152 participants) were included. 100 studies including 16 812 participants and 30 antipsychotics contributed to our network meta-analysis of the primary outcome. All antipsychotics had risk ratios (RRs) less than 1·00 when compared with placebo for relapse prevention and almost all had 95% credible intervals (CrIs) excluding no effect. RRs ranged from 0·20 (95% CrI 0·05–0·41) for paliperidone oral to 0·65 (0·16–1·14) for cariprazine oral (moderate-to-low confidence in estimates). Generally, we interpret that there was no clear evidence for the superiority of specific antipsychotics in terms of relapse prevention because most comparisons between antipsychotics included a probability of no difference.

Interpretation: As we found no clear differences between antipsychotics for relapse prevention, we conclude that the choice of antipsychotic for maintenance treatment should be guided mainly by their tolerability.

Funding: The German Ministry of Education and Research and Oxford Health Biomedical Research Centre.

Siva Nayanah. Gilead and ViiV Healthcare reach settlement over HIV drug. *Lancet 2022;*399(10325): 618p.

Tatum Megan. Escalating threats to health workers in Myanmar. *Lancet 2022;*399(10325): 619p.

Theodoropoulos Konstantinos C, Liakopoulou Alexandra, Tsagkaropoulos Sokratis, Kassimis George, Anastasiadis Kyriakos. Under-sensing by a temporary pacemaker after cardiac surgery and ventricular fibrillation. *Lancet 2022;*399(10325): 677p.

Thornton Jacqui. Ambitious UK plans on levelling up lack detail and funding. *Lancet 2022;*399(10325): 617p.

Tromp Tycho R, Hartgers Merel L, Hovingh G Kees, Antonio J Vallejo Vaz, Cuchel Marina. Worldwide experience of homozygous familial hypercholesterolaemia: Retrospective cohort study. *Lancet 2022;*399(10326): 719-28p.

Abstract:

Background: Homozygous familial hypercholesterolaemia (HoFH) is a rare inherited disorder resulting in extremely elevated low-density lipoprotein cholesterol levels and premature atherosclerotic cardiovascular disease (ASCVD). Current guidance about its management and prognosis stems from small studies, mostly from high-income countries. The objective of this study was to assess the clinical and genetic characteristics, as well as the impact, of current practice on health outcomes of HoFH patients globally.

Methods: The HoFH International Clinical Collaborators registry collected data on patients with a clinical, or genetic, or both, diagnosis of HoFH using a retrospective cohort study design. This trial is registered with ClinicalTrials.gov, NCT04815005.

Findings: Overall, 751 patients from 38 countries were included, with 565 (75%) reporting biallelic pathogenic variants. The median age of diagnosis was 12·0 years (IQR 5·5–27·0) years. Of the 751 patients, 389 (52%) were female and 362 (48%) were male. Race was reported for 527 patients; 338 (64%) patients were White, 121 (23%) were Asian, and 68 (13%) were Black or mixed race. The major manifestations of ASCVD or aortic stenosis were already present in 65 (9%) of patients at diagnosis of HoFH. Globally, pretreatment LDL cholesterol levels were 14·7 mmol/L (IQR 11·6–18·4). Among patients with detailed therapeutic information, 491 (92%) of 534 received statins, 342 (64%) of 534 received ezetimibe, and 243 (39%) of 621 received lipoprotein apheresis. On-treatment LDL cholesterol levels were lower in high-income countries (3·93 mmol/L, IQR 2·6–5·8) versus non-high-income countries (9·3 mmol/L, 6·7–12·7), with greater use of three or more lipid-lowering therapies (LLT; high-income 66% vs non-high-income 24%) and consequently more patients attaining guideline-recommended LDL cholesterol goals (high-income 21% vs non-high-income 3%). A first major adverse cardiovascular event occurred a decade earlier in non-high-income countries, at a median age of 24·5 years (IQR 17·0–34·5) versus 37·0 years (29·0–49·0) in high-income countries (adjusted hazard ratio 1·64, 95% CI 1·13–2·38).

Interpretation: Worldwide, patients with HoFH are diagnosed too late, undertreated, and at high premature ASCVD risk. Greater use of multi-LLT regimens is associated with lower LDL cholesterol levels and better outcomes. Significant global disparities exist in treatment regimens, control of LDL cholesterol levels, and cardiovascular event-free survival, which demands a critical re-evaluation of global health policy to reduce inequalities and improve outcomes for all patients with HoFH.

Funding: Amsterdam University Medical Centers, Location Academic Medical Center; Perelman School of Medicine at the University of Pennsylvania; and European Atherosclerosis Society

Wykoff Charles C, Abreu Francis, Adamis Anthony P, Basu Karen, Zheutlin Jeffrey. Efficacy, durability, and safety of intravitreal faricimab with extended dosing up to every 16 weeks in patients with diabetic macular oedema (YOSEMITE and RHINE): Two randomised, double-masked, phase 3 trials. ***Lancet 2022;*****399(10326): 741-55p.**

Abstract:

Background: To reduce treatment burden and optimise patient outcomes in diabetic macular oedema, we present 1-year results from two phase 3 trials of faricimab, a novel angiopoietin-2 and vascular endothelial growth factor-A bispecific antibody.

Methods: YOSEMITE and RHINE were randomised, double-masked, non-inferiority trials across 353 sites worldwide. Adults with vision loss due to centre-involving diabetic macular oedema were randomly assigned (1:1:1) to intravitreal faricimab 6·0 mg every 8 weeks, faricimab 6·0 mg per personalised treatment interval (PTI), or aflibercept 2·0 mg every 8 weeks up to week 100. PTI dosing intervals were extended, maintained, or reduced (every 4 weeks up to every 16 weeks) based on disease activity at active dosing visits. The primary endpoint was mean change in best-corrected visual acuity at 1 year, averaged over weeks 48, 52, and 56. Efficacy analyses included the intention-to-treat population (non-inferiority margin 4 Early Treatment Diabetic Retinopathy Study [ETDRS] letters); safety analyses included patients with at least one dose of study treatment. These trials are registered with ClinicalTrials.gov (YOSEMITE NCT03622580 and RHINE NCT03622593).

Findings: 3247 patients were screened for eligibility in YOSEMITE (n=1532) and RHINE (n=1715). After exclusions, 940 patients were enrolled into YOSEMITE between Sept 5, 2018, and Sept 19, 2019, and 951 patients were enrolled into RHINE between Oct 9, 2018, and Sept 20, 2019. These 1891 patients were randomly assigned to faricimab every 8 weeks (YOSEMITE n=315, RHINE n=317), faricimab PTI (n=313, n=319), or aflibercept every 8 weeks (n=312, n=315). Non-inferiority for the primary endpoint was achieved with faricimab every 8 weeks (adjusted mean vs aflibercept every 8 weeks in YOSEMITE 10·7 ETDRS letters [97·52% CI 9·4 to 12·0] vs 10·9 ETDRS letters [9·6 to 12·2], difference −0·2 ETDRS letters [−2·0 to 1·6]; RHINE 11·8 ETDRS letters [10·6 to 13·0] vs 10·3 ETDRS letters

[9·1 to 11·4] letters, difference 1·5 ETDRS letters [−0·1 to 3·2]) and faricimab PTI (YOSEMITE 11·6 ETDRS letters [10·3 to 12·9], difference 0·7 ETDRS letters [−1·1 to 2·5]; RHINE 10·8 ETDRS letters [9·6 to 11·9], difference 0·5 ETDRS letters [−1·1 to 2·1]). Incidence of ocular adverse events was comparable between faricimab every 8 weeks (YOSEMITE n=98 [31%], RHINE n=137 [43%]), faricimab PTI (n=106 [34%], n=119 [37%]), and aflibercept every 8 weeks (n=102 [33%], n=113 [36%]).

Interpretation: Robust vision gains and anatomical improvements with faricimab were achieved with adjustable dosing up to every 16 weeks, demonstrating the potential for faricimab to extend the durability of treatment for patients with diabetic macular oedema.

Funding: F Hoffmann-La Roche.

Zarocostas John. WHO concerned over COVID-19 health-care waste. *Lancet 2022;*399(10324): 507p.