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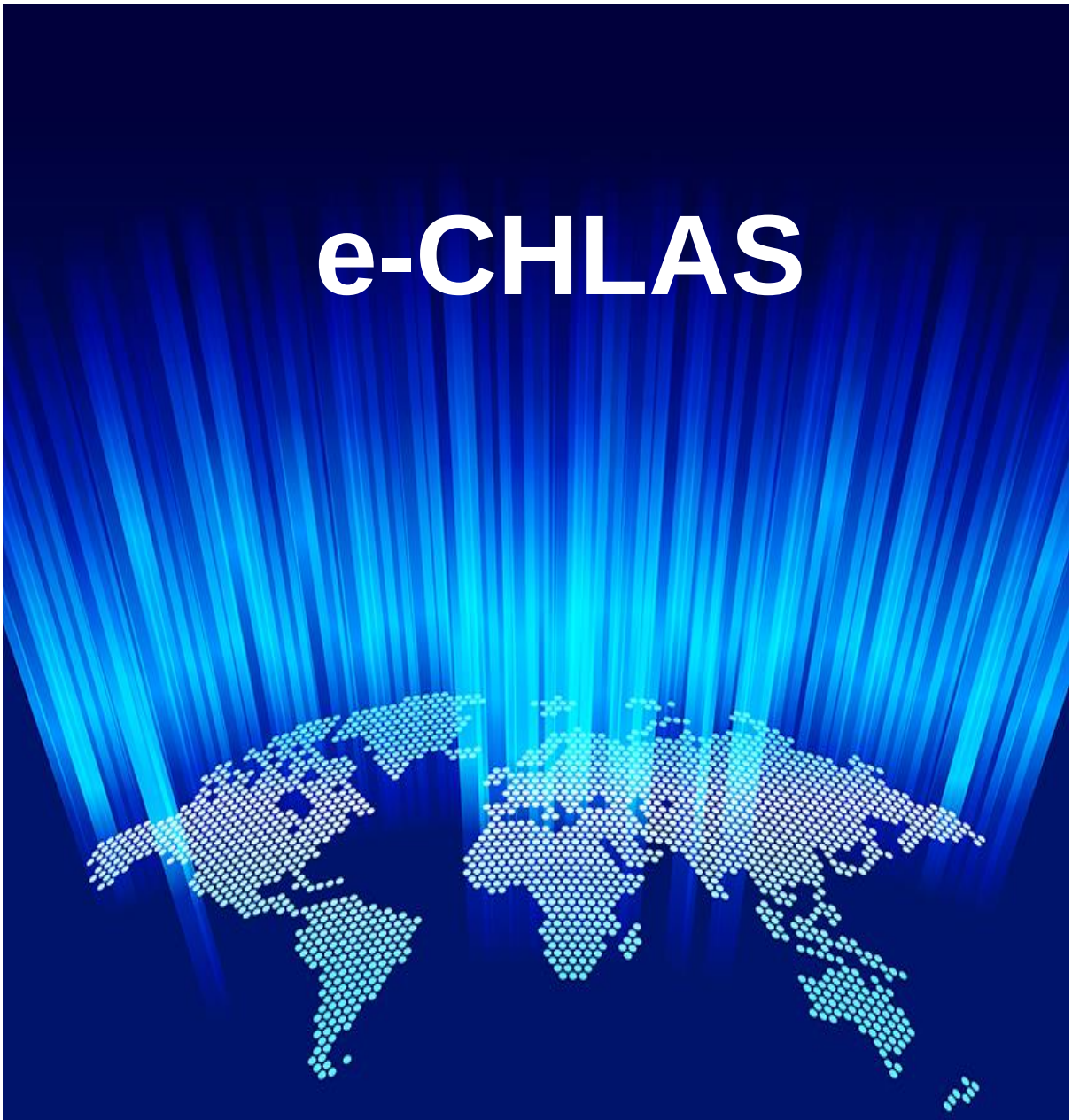

MARCH 2022

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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.

(Dr. O.P. Verma)
Librarian

AYUSH & Other System

Alschuler Lise, Chiasson Ann Marie, Horwitz Randy, Sternberg Esther, Maizes Victoria. Integrative medicine considerations for convalescence from mild-to-moderate COVID-19 disease. *Explore: 2022;* 18(2): 140-48p.

Abstract:

The majority of individuals infected with SARS-CoV-2 have mild-to-moderate COVID-19 disease. Convalescence from mild-to-moderate (MtoM) COVID-19 disease may be supported by integrative medicine strategies. Integrative Medicine (IM) is defined as healing-oriented medicine that takes account of the whole person, including all aspects of lifestyle. Integrative medicine strategies that may support recovery from MtoM COVID-19 are proposed given their clinically studied effects in related conditions. Adoption of an anti-inflammatory diet, supplementation with vitamin D, glutathione, melatonin, Cordyceps, Astragalus and garlic have potential utility. Osteopathic manipulation, Qigong, breathing exercises and aerobic exercise may support pulmonary recovery. Stress reduction, environmental optimization, creative expression and aromatherapy can provide healing support and minimize enduring trauma. These modalities would benefit from clinical trials in people recovering from COVID-19 infection.

Bastos Marco Aurelio Vinhosa, Bastos Paulo Roberto Haidamus Oliveira, Filho Geraldo Barbosa Foscaches, Conde Ricardo Brilhante, Lucchetti Giancarlo. Corpus callosum size, hypnotic susceptibility and empathy in women with alleged mediumship: A controlled study. *Explore: 2022;* 18(2): 217-25p.

Abstract:

Aim: Evidence indicates that highly hypnotizable subjects may have larger area of the rostrum of the corpus callosum (CC). Mediumship can be defined as the alleged ability to communicate regularly with deceased personalities, and self-hypnosis is postulated as an underlying mechanism for this ability. Therefore, we aimed to investigate the CC area, hypnotic susceptibility, self-reported dissociation, and empathy in alleged mediums in comparison with healthy, non-medium controls.

Methods: The study sample consisted of 16 Spiritist mediums (medium group (MG)) and 16 non-medium controls. Magnetic resonance imaging scans were performed to measure the CC areas (total and subdivisions). The Harvard Group Scale of Hypnotic Susceptibility was used to assess hypnotizability, and self-reported measures were used to investigate anomalous experiences, mental health using the Self-Reporting Questionnaire-SRQ, dissociative experiences using the Dissociative Experiences Scale, and empathy using the Interpersonal Reactivity Index.

Results: No between-group differences were found in the total or subdivided CC areas or in hypnotizability, with both groups showing intermediate levels. The rostrum of the CC area and hypnotizability were not correlated. The MG presented with significantly more anomalous experiences, but the two groups had similar scores for dissociation, empathy, and mental health.

Conclusion: The normal CC areas found in the MG are in contrast with the abnormal results typically observed in subjects with psychotic and dissociative disorders. Although hypnotizability was not different between groups, further studies are needed to replicate these findings in other samples.

Chang Tracy FH, Ramburn Triya T, Pundir Sheetal, Purandare Pradeep, Subramaniam Balachundhar. Effect of the Inner Engineering Online Program as a Positive Intervention on Subjective Well-Being and Positive Work Outcomes. ***Journal of Integrative and Complementary Medicine 2022;*** **28(3): 278-82p.**

Abstract:

Objective: This study evaluates the effect of Inner Engineering Online (IEO) on subjective well-being and positive work outcomes.

Design: The study uses a field quasi-experimental one group design with pre- and post-tests.

Interventions: IEO is a multicomponent online self-paced program. The program consists of seven online sessions to be completed over a 4-week period.

Results: The study finds that IEO has a positive effect on subjective well-being (mindfulness, joy, vitality, restfulness, and oneness) and positive work outcomes (meaningful work, psychological capital, and work engagement).

Conclusion: The findings on IEO have important practical implications for improving subjective well-being and work experiences.

Chhikara Jyoti, Singh Rahul. Individualized homeopathy in a case of liver abscess: A case report. ***Indian Journal of Research in Homoeopathy: 2022;*** **16(1): 55-60p.**

Abstract:

Introduction: Liver abscesses (LAs) are purulent collections in the liver parenchyma that result from bacterial, fungal, or parasitic infection which can spread to the liver by extension of an adjacent infection, or as a result of trauma. Homoeopathic approach of treating the disease based on symptom totality is a relevant alternative to often unsatisfactory conventional medicine in cases of LA.

Case Summary: A 35-yearold male who presented with LA was treated with homoeopathic medicine based on the totality of symptoms and significant improvement was seen with resolution of abscess in the liver along with relief in other presenting symptoms. This enhances our belief in the potential of individualized homeopathy in treating infectious conditions.

Choubey Gurudev, Nahar Laijun, Banerjee Abhiram, Roja Varanasi. Role of homoeopathy in the management of adhesive capsulitis: A pretest-posttest study. *Indian Journal of Research in Homoeopathy: 2022;* 16(1): 31-40p.

Abstract:

Background: Adhesive capsulitis (AC) is an insidious and painful stiffening of the glenohumeral (shoulder) joint, resulting in compromised functional ability and quality of life (QoL). Objectives: Primary objective was to evaluate change in shoulder pain after individualised homoeopathy treatment for over 2 months. Secondary objective was to assess the change in the QoL and outcome related to impact on daily living (ORIDL).

Methods: A single-arm, pretest-posttest, clinical study on AC was conducted on 40 participants recruited from the outpatient clinic of rheumatological disorders at Clinical Research Unit (Homoeopathy), Siliguri, West Bengal, India. Medicines were prescribed on the basis of the totality of symptoms. Changes in shoulder pain over 2 months were evaluated using the shoulder pain and disability index (SPADI). QoL was evaluated using SF-12v2 and ORIDL (participants and physician assessed), respectively.

Results: Thirty-six participants completed the study and four participants dropped out. A protocol compliant sample of n = 36 was analysed. There was a statistically significant reduction of SPADI score (91.92 ± 10.22 vs. 34.14 ± 24.43; mean reduction 57.78, 95% CI 49.41–66.14, P < 0.001) and statistically significant increase in SF-12 v2 score (44.39 ± 9.70 vs. 72.27 ± 10.97; mean increase 27.87, 95% CI 23.89–31.85, P < 0.001). The Spearman's correlation between the changes in physician assessment ORIDL scores and participants assessment ORIDL scores over 2 months suggested a statistically significant correlation (rs = 0.998, P < 0.01).

Conclusion: The findings showed symptom alleviation, and improvement in the QoL after homoeopathic treatment. Randomised controlled trials are further warranted.

Clinical case reports: A time-tested, traditional way to enhance evidence. *Indian Journal of Research in Homoeopathy: 2022;* 16(1): 1-2p.

Collins David, Shamblen Steve, Rindfleisch Adam, Hollifield Michael. Evaluation of a Veterans Health Administration Whole Health for Mental

Health Course for Clinicians. *Journal of Integrative and Complementary Medicine 2022;* 28(3): 261-67p.

Abstract:

Objectives: Veterans experience mental health disorders at higher rates than their civilian counterparts and also experience multiple barriers to mental health services. The Veterans Health Administration (VA) has implemented a Whole Health approach to make health care more person-focused and oriented toward promotion of health-sustaining behavior. We conducted an evaluation to investigate the effects of a Whole Health for Mental Health (WHMH) course for clinicians that focuses on shifting the perspective to a system of care in which mental health is incorporated as a core part of whole-person care.

Design: We collected surveys before the course, immediately after the course, and at a 2-month follow-up.

Settings/Location: The course was implemented in non-clinical settings in two VA medical centers (one in the Northeast and one in the Mountain West).

Subjects: Our sample consisted of VA staff who enrolled in WHMH and completed a pre- and post-survey (n = 100) and follow-up survey (n = 99).

Intervention: The WHMH is a 2-day face-to-face course that covers multiple aspects of mental health through a Whole Health lens. The course includes evidence-based practices within each aspect of mental health. The course also emphasizes implementation of Whole Health in clinicians' lives, their practice, and the health care system.

Outcome measures: Attitudes were measured at pre-, post-, and follow-up assessments. The WHMH behaviors were measured at pre- and follow-up assessments.

Results: There were statistically significant, large changes toward improvement from pre-test to post-test for all attitudes examined. These changes remained significant at follow-up, and the magnitude of change remained at least medium to large. Statistically significant, medium magnitude or larger improvements were found at follow-up for four of the five WHMH behavior outcomes examined.

Conclusions: Our results suggest that clinicians can increase their attitudes and use of Whole Health concepts and both conventional and complementary approaches related to mental health issues.

Demarinis Susie. Underdiagnosed food allergies in children on Medicaid. *Explore: 2022;* 18(2): 134-35p.

Dincer Berna, Ozçelik Semanur Kumral, Ozer Zulfunaz, Bahçecik Nefise. Breathing therapy and emotional freedom techniques on public speaking anxiety in Turkish nursing students: A randomized controlled study. *Explore: 2022;* 18(2): 226-33p.

Abstract:

Background and objective: Public speaking is a common challenge that university students have to face. This study aims to determine the effects of Breathing Therapy and Emotional Freedom Techniques (EFT) on public speaking anxiety in Turkish nursing students.

Methods: This randomized controlled study included 76 nursing students. Data were collected using the Descriptive Characteristics Form, Subjective Units of Disturbance Scale, The State-Trait Anxiety Inventory, and the Speech Anxiety Scale.

Results: Before the administration of Breathing Therapy and EFT, the students' median scores from the Subjective Units of Disturbance Scale, the State-Trait Anxiety Inventory, and the Speech Anxiety Scale were similar. However, the median scores of the Subjective Units of Disturbance Scale, the State-Trait Anxiety Inventory, and the Speech Anxiety Scale scores significantly decreased in both of the experimental groups after the interventions ($p < 0.001$). EFT ($d = 3.18$) was more effective than Breathing Therapy ($d = 1.46$) in reducing Speech anxiety.

Conclusion: It was found that Breathing Therapy and EFT are effective methods to reduce stress, anxiety, and speaking anxiety.

Escola Gascon Alex. Forced-choice experiment on Anomalous Information Reception and correlations with states of consciousness using the Multivariable Multiaxial Suggestibility Inventory-2 (MMSI-2). *Explore: 2022;* 18(2): 170-78p.

Abstract:

Context: An Anomalous Information Reception (AIR) experiment was developed.

Objective: To statistically examine the occurrence of AIR in multiple experimental tests and explore their predictive psychological mechanisms.

Design: First, we investigated whether human beings could guess the positive or negative content from 30 randomly selected images that would be presented on a computer screen, one at a time. Ninety participants reported being mediums and another 90 claimed to be nonbelievers in the paranormal. The participants were randomly assigned to three experimental conditions: (1) positive-relaxing environments, (2) neutral environments, and (3) negative-stimulating environments. Second, the prediction of successes recorded in the AIR experiment was tested using five Multivariable Multiaxial Suggestibility Inventory-2 (MMSI-2) scales that measured the altered state of consciousness (ASC) and suggestibility.

Results: The successes did not exceed the estimated chance. The only significant results revealed that mediums obtained a greater number of correct answers than the non-believing participants. Bayesian estimation also confirmed these results. In the same way, the altered states of consciousness and suggestibility negatively predicted 25.8% of successes in the AIR experiment.

Conclusions: Insufficient statistical evidence was obtained for AIR. The results raise doubts about previous theories on AIR. Further research is required. Nevertheless, mediums obtained more success answers than nonbelievers did. This means that the anomalous sheep-goat effect is also present in mediums and supports results obtained in previous studies.

Feng Qian, Chen Yu, Wang Lin, Li Mengmei, Bai Xuemei. Effect of information fields from written texts on cell growth and mitochondrial functions in-vitro: An exploratory study. *Explore: 2022;* 18(2): 205-09p.

Abstract:

Objective: Mitochondria are considered a portal to receive, process and integrate external energy and information to maintain cellular homeostasis. We examined the effect of Chinese texts with positive and negative meaning on the growth and mitochondrial functions using a mouse kidney collecting duct cell line called M1 cells.

Methods: To avoid skewing the results due to differential handling of the cells or analyzing the results, we conducted experiments by keeping the texts and blanks covered in brown opaque envelopes, exposed the cells to randomly selected envelopes and examined the differences over time. All operators involved in the experiments did not know the contents of the envelopes until the end of the experiments, and all data are expressed relative to the controls.

Results: Cell growth rate was not affected for the group treated with positive information but was significantly reduced by 18% when treated with negative information. At the biochemical level, positive texts significantly increased whole cell adenosine triphosphate (ATP) and glutathione (GSH) by 22% and 21% respectively.

Conclusions: This study for the first time demonstrated the effect of written words on specific biochemical measures in cultured mammalian cells.

Hartman Laurie J. Dietary interventions for multiple sclerosis-related outcomes: Summary of a cochrane review. *Explore: 2022;* 18(2): 252-53p.

Her Ladda, Kanjanasilp Juntip, Chaiyakunapruk Nathorn, Sawangjit Ratree. Efficacy and Safety of Eucalyptus for Relieving Cough: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Journal of Integrative and Complementary Medicine 2022;* 28(3): 218-26p.

Abstract:

Objectives: To assess the efficacy and safety of Eucalyptus globulus Labill (Eucalyptus) on cough.

Background: Cough is a common symptom of upper respiratory tract infections (URTIs) and bronchitis. Eucalyptus products are frequently used as over-the-counter cough medications but their efficacy and safety are uncertain.

Methods: Randomized controlled trials (RCTs) investigating efficacy and safety of Eucalyptus for cough were systematically searched in electronic databases till February 2021. Two reviewers independently performed study selection, data extraction, and quality assessment. Clinical outcomes including improvement or resolution of overall cough symptoms, cough frequency (CF), and adverse events (AEs) of Eucalyptus were evaluated and analyzed using a random-effects model. Heterogeneity was evaluated using I2 and chi-squared test.

Results: Six RCTs with 1,857 participants with cough were included in this study. Most of the included studies used Eucalyptus in combination formula (four of six studies). Based on Cochrane's risk of bias criteria, three of six studies (50%) were rated low risk of bias, whereas the remaining were judged as high risk of bias. This study found that Eucalyptus products are more effective than placebo in terms of improvement or resolution of overall cough symptoms with relative risk 1.45 (95% confidence interval (95% CI) 1.26–1.67). Whereas all Eucalyptus formulae reduced CF with weighted mean difference 0.44 (95% CI 0.28–0.60), when compared with placebo. There are no serious AEs associated with Eucalyptus during treatment periods. Mild-to-moderate gastrointestinal symptoms were common AEs reported in a comparable study between Eucalyptus and control groups.

Conclusion: The findings indicate that Eucalyptus products are safe for use in cough related to respiratory diseases such as URTIs and bronchitis. However, their efficacy is minimal and of uncertain clinical importance. Further high-quality studies are still necessary to confirm this finding.

Kırca Ayça Şolt, Gul Derya Kanza. Effect of music and skin contact with the newborn on pain and anxiety during episiotomy repair in primiparous women: A double-blind randomized controlled study. *Explore: 2022;* 18(2): 210-16p.

Abstract:

Objective: To show that music medicine and skin contact with the newborns can reduce pain and anxiety during episiotomy repair.

Design: Double-blind randomized controlled trial

Setting: The study was conducted between April and July 2020 at the private Medipol Nisa Hospital.

Participants: A total of 150 primiparous pregnant women over 20 years of age who underwent vaginal delivery with episiotomy

Interventions: Participants were randomized into the music medicine, skin contact with the newborn, and control groups (with no treatment). After episiotomy repair (with the designated treatment or no treatment), the State Trait Anxiety Inventory and Visual Analog Scale were used to assess anxiety and pain, respectively.

Main outcome measures: Pain and anxiety experienced after episiotomy repair in the treatment and control groups.

Results: Women in both treatment groups (music medicine and skin-to-skin contact) had significantly lower anxiety and pain levels than those in the control group. In particular, music medicine significantly reduced pain in comparison to skin contact with the newborn (VAS 2 3.92 ± 1.46 vs. 5.42 ± 1.73, respectively, VAS 3 2.64 ± 1.63 vs. 5.14 ± 1.77, respectively, VAS 4 1.38 ± 1.46 vs. 4.14 ± 2.04, respectively, $p < 0.05$). Thus, music medicine is more effective than skin-to-skin contact in reducing the pain experienced during episiotomy repair, but both treatments were equally effective in reducing anxiety (35.30 ± 6.47 vs. 36.82 ± 9.71 vs. 49.22 ± 16.95, respectively, $p < 0.05$).

Conclusion: Both of these nonpharmacological treatments can be used along with analgesics and anxiolytics for the treatment of pain and anxiety during episiotomy repair.

Klatt Maryanna, Westrick Alexis, Bawa Rani, Gabram Olivia, Emerson Brent. Sustained resiliency building and burnout reduction for healthcare professionals via organizational sponsored mindfulness programming. *Explore: 2022;* 18(2): 179-86p.

Abstract:

Purpose: To measure healthcare professional (HCP) result sustainability following implementation of an organizationally sponsored Mindfulness Based Intervention (MBI), Mindfulness in Motion (MIM), in areas of burnout, perceived stress, resilience, and work engagement.

Methods: A follow-up survey was sent via email to healthcare professionals (n = 220) who previously participated in the 8-week MIM intervention. Survey assessed burnout, perceived stress, resilience, work engagement, and included open-ended questions pertaining to barriers, facilitators, and sustained impact of practicing mindfulness after program end.

Results: Analysis included 66 healthcare professionals with sustainability time frames ranging from 3 to 28 months from initial program finish. Average time since intervention end was 12.2 months. Based on 12.2 months sustained results post MIM, there were significant differences from pre-MIM to sustainability follow-up in burnout (*p = 0.0047), perceived stress (*p = 0.00001), and resilience (*p = 0.0004). Work engagement benefits were non-significant from pre-test to follow-up (p = 0.4008). There were no significant differences in results when comparing the length of time since participant was enrolled in the initial study. Additionally, analysis of the qualitative data revealed multiple subthemes relating to facilitators of sustained mindfulness, barriers to practicing mindfulness, and lasting impacts of the MIM intervention.

Conclusions: For Healthcare Professionals, the organizationally sponsored mindfulness intervention outcomes were sustained beyond the 8-weeks of the initial MIM intervention for all but one outcome variable. Post 8–week intervention end, participants were given the option of receiving weekly "Mindful Moment" emails and attending monthly mindfulness booster sessions. Organizational support may be a pivotal factor in sustaining positive results achieved via mindfulness programming.

Koch Steven, Esch Tobias, Werdecker Lena. Effects of a Yoga-Based Stress Intervention Program on the Blood Pressure of Young Police Officers: A Randomized Controlled Trial. *Journal of Integrative and Complementary Medicine 2022;* 28(3): 234-40p.

Abstract:

Objectives: Despite improvements in health education and treatment, arterial hypertension remains a major health problem of increasing epidemiological importance. The purpose of this randomized controlled trial was to determine the impact of regular yoga breathing exercises on blood pressure, work-related stress, and the prevalence of arterial hypertension in young police academy trainees with no existing comorbidities.

Design: A single-center, prospective, randomized controlled trial.

Subjects: The study included 120 healthy trainees aged between 18 and 39 years who practiced weekly yoga exercises with an emphasis on breathing (prāṇāyāma) over an observation period of 6 months.

Results: These regular exercises lowered the blood pressure of the participants by 1.34 mmHg (right arm, $p = 0.007$), increased their regenerative capacity (Recovery Experience Questionnaire [REQ] scale +2.77, $p < 0.001$) and resilience (Resilience Scale [RS] +4.6, $p = 0.001$), and concomitantly reduced the level of perceived stress (Perceived Stress Scale [PSS] −0.9, $p < 0.001$). In contrast, blood pressure in the control group had slightly increased over the study period by 0.1 mmHg (right arm, $p < 0.001$) and 1.0 mmHg (left arm, $p = 0.03$), and subjective scores had significantly worsened (REQ scale −3.4, $p < 0.001$; RS −2.29, $p = 0.001$; PSS +0.88, $p < 0.001$).

Conclusions: The results point to a significant correlation between blood pressure and both regenerative capacity and stress level. Thus, the study confirms the hypothesis that yoga exercises reduce perceived stress and exert positive effects on blood pressure.

Leskowitz Eric. Cartography of energy medicine: From subtle anatomy to energy physiology. *Explore: 2022;* 18(2): 152-64p.

Abstract:

The field of energy medicine (EM) is perhaps the most controversial branch of integrative medicine. Its core concept - the existence of an invisible healing energy – has not yet been validated by Western medicine, and the mechanism(s) of action of its techniques have not been fully elucidated. This paper addresses these problems by marshalling several types of evidence: basic science research into electromagnetic fields (EMF), subjective sensations experienced when receiving EM treatments, and clairvoyant perceptions of EM in action. The latter two sources of information, while not solid enough to meet current standards of scientific rigor, can nonetheless generate important new information. A hypothesis is then developed to explain these findings.

First, the main components of the human subtle energy system are presented: the “subtle anatomy” of the meridians, of the energy centers and of the biofield. Several representative EM techniques are then analyzed to determine which specific components of that energy structure they impact. Next, EM's mechanisms of action are explored by describing how these altered energy dynamics can affect biologic processes. This subject is termed “energy physiology”, in parallel with conventional medicine's foundation in anatomy and physiology. Finally, potential research into energy physiology is outlined that focuses on several common but distinctive experiences which are not fully explained by the current mechanistic biomedical model. Plausible and testable energy-based explanations are proposed for phantom limb pain, emotional entrainment in groups, unusually rapid symptom

response to EM, and the invisible templates that guide cell growth and differentiation.

This analysis is intended to serve as a guide to future clinical and research explorations into the multidimensional nature of human beings. As Western medicine develops technologies that can generate objective empiric evidence in these subtle domains, we will be able to more fully understand the energetic components of health and illness.

Mehra Pritha, Sahoo Amulya Ratna, Rajakumar BSJ, Singh Jai P, Arya BS. Homoeopathic pathogenetic trial of Mentha piperita L.: A multicentric, double-blind, randomised and placebo-controlled trial. *Indian Journal of Research in Homoeopathy: 2022;* 16(1): 3-20p.

Abstract:

Introduction: Mentha piperita L, a lesser-known and partly proved drug in homoeopathy, is used extensively as a herbal medicine.

Objective: The objective of this study is to elicit the pathogenetic response of Mentha piperita in comparison to placebo.

Materials and Methods: A multicentre, double-blind, placebo-controlled and randomised clinical trial was carried out at three centres with 46 relatively healthy provers. After randomisation, 32 provers were given verum in 6C, 12C, 30C and 200C potencies and in the placebo group,14 provers were administered identical, un-medicated globules. All the changes were recorded by the provers and elaborated by proving masters. The data were finally processed at proving-cum-data processing cell.

Results: Out of the 32 provers of the Verum group, 22 reported 61 symptoms, whereas 24 symptoms were reported by seven provers in the placebo group. The majority of the symptoms were produced in the sphere of the locomotor system, followed by the gastro-intestinal system beside other systems. Altogether, ten new Grade I symptoms were identified, while 11 symptoms were similar to those found in the previous literature.

Conclusion: Mentha piperita revealed a significant pathogenetic response in this trial which verifies its previously observed symptoms. Among the newly developed symptoms, two symptoms showed opposite character when compared to the previous literature. Also, statistically significant difference was found in differential eosinophil count in the verum group pre-post intervention. These are the findings that need to be clinically verified to enhance the scope of their clinical use**.**

Mitarnun Witoon, Mitranun Witid, Mitarnun Wenika, Pangwong Wilasinee. Home-Based Walking Meditation Decreases Disease Severity in Parkinson's Disease: A Randomized Controlled Trial. *Journal of Integrative and Complementary Medicine 2022;* 28(3): 227-33p.

Abstract:

Objective: To determine the effects of walking meditation (WM) on functional performance, disease severity, and anxiety in Parkinson's disease (PD).

Design: This was a randomized controlled trial.

Settings: The study was conducted at a regional hospital.

Subjects/Interventions: Thirty-three participants with PD were randomly allocated to the control (CON) group (n = 16) or the WM group (n = 17). Participants in the WM group were asked to perform WM monthly under supervision and encouraged to practice at home at least 3 days/week for 12 weeks.

Outcome measurements: Gait velocity, Timed Up and Go, five times sit to stand (FTSTS) test, Unified Parkinson's Disease Rating Scale (UPDRS), and the percentage of participants with anxiety (Hospital Anxiety and Depression Scale–part anxiety [HADS-A] ≥8).

Results: Both groups showed reduced gait velocity ($p < 0.05$), although impairment of the FTSTS ($p < 0.05$) score was observed only in the CON group. A significant enhancement within and between groups in the total UPDRS and UPDRS part II scores was observed only in the WM group. The percentage of participants with anxiety (HADS-A ≥ 8) decreased significantly only in the WM group ($p < 0.05$), compared with the baseline and after 12 weeks. There was no loss to follow-up in the WM group, and the participation rate of training was 3.2 days/week.

Conclusions: Home-based WM can encourage high rates of exercise adherence, reduce disease severity, lower the percentage of participants with anxiety, and might be suitable during disease endemic and/or pandemic in PD.

Mohammadi Roghayeh, Javanmard Gholam Hossein, Alipour Ahmad, Zare Hossein. Effects of mindful breath awareness and muscle relaxation and transcranial electrical stimulation techniques on improving blood pressure status in patients with type 2 diabetes. *Explore: 2022;* 18(2): 200-04p.

Abstract:

Objective: The present study aimed to determine the effects of mindful breath awareness & muscle relaxation (MBMR) and transcranial electrical stimulation (tCES) techniques on improving the systolic and diastolic blood pressure status in patients with type 2 diabetes.

Methods: The research method was randomized controlled trial (RCT) using split-plot ANOVA (SPANOVA). Thirty patients were selected through purposive sampling from Bonab County Diabetes Association (Iran) and were

randomly divided into three 10-member groups, namely MBMR, tCES, and MBMR+tCES groups. Participants received their group interventions in 10 individual sessions. All patients were evaluated for systolic and diastolic blood pressure at two stages, before and immediately after each session. SPANOVA and Bonferroni pairwise comparison tests were used for data analysis.

Results: The results indicated that the MBMR and tCES techniques, alone and in combination, had significant and equal effects on reducing diastolic blood pressure, but the MBMR treatment was more effective in the systolic blood pressure than the tCES.

Conclusions: The MBMR and tCES techniques were effective and safe in treating hypertension in patients with type 2 diabetes.

Moonaz S, Whitehead AM, Lawrence L, Natividad D, Teets R. Yoga therapy DYADS: A novel approach to chronic pain management in underserved populations. *Explore: 2022;* 18(2): 195-99p.

Abstract:

Yoga therapy is an emerging integrative health approach that applies the practices and teachings of yoga for individuals with clinical concerns. It is generally offered as individual sessions between a yoga therapist and client or in a small group setting with several clients who share a clinical concern. Here we describe a third model for consideration- the yoga therapy dyad. A dyad includes two clients working simultaneously with a single yoga therapist and differs from both individual and small group sessions in the potential benefits and challenges. The yoga therapy dyad model that is detailed here was implemented as part of a feasibility trial along with group acupuncture therapy for chronic pain in an underserved population. Underserved populations are at risk for pain and reduced access to care. This pilot may inform future research, policy, education, and clinical practice.

Noh Je Heon, Byun Da young, Han Si hoon, Kim Jeongyoon, Ha In Hyuk. Effectiveness and safety of motion style acupuncture treatment of the pelvic joint for herniated lumbar disc with radiating pain: A prospective, observational pilot study. *Explore: 2022;* 18(2): 240-49p.

Abstract:

Context: Conservative treatment is effective for treating and managing herniated lumbar disc with radiating leg pain.

Objectives: To investigate the effects of motion style acupuncture treatment (MSAT) on the pelvic joint for this condition.

Design: This prospective observational study was a pilot study for a future randomized, controlled trial (RCT).

Setting: masked for review.

Patients/Interventions: We enroled 40 patients and allocated them to two groups (both n = 20). Groups 1 and 2 received integrative Korean medicine treatment (KMT) and integrative KMT with MSAT for pelvic joint, respectively. Primary outcome was the Numeric Rating Scale (NRS) score for low back pain. Secondary outcomes were the Oswestry Disability Index (ODI), Visual analogue Scale (VAS), and EuroQol 5-Dimension-5-level (EQ-5D-5 L) scores. Efficacy was assessed by comparing the baseline and Day 4 results. Safety was assessed based on the frequency and severity of all adverse events.

Results: On Day 14, except for ODI in Group 1, the NRS, VAS, and EQ-5D-5 L scores showed significant improvements in both groups. On Day 90, both groups showed significant improvements in the NRS, ODI, and EQ-5D-5 L scores. There was a significant between-group difference in the NRS score on Day 7. On Day 14, Group 2 had a significantly lower VAS score for radiating leg pain than Group 1. Twelve patients reported adverse events associated with integrative KMT; however, there was no association with pelvic joint MSAT.

Conclusion: Adding MSAT for pelvic joint to conventional integrative KMT may ameliorate radiating leg pain and improve the quality of life.

Pintas Stephanie, Zhang Annie, James Kevin J, Lee Roger M, Shubov Andrew. Effect of Inpatient Integrative Medicine Consultation on 30-Day Readmission Rates: A Retrospective Observational Study at a Major U.S. Academic Hospital. *Journal of Integrative and Complementary Medicine 2022;* 28(3): 241-49p.

Abstract:

Objectives: The prevalence of inpatient integrative medicine (IM) consult services is increasing among academic health care institutions. The diversity of services between institutions, as well as the novel nature of such interventions, makes it challenging for health care administrators to determine the cost/benefit of adding such a program to their institution. The main purpose of this study was to examine the performance of the new University of California, Los Angeles (UCLA) East-West (EW) consult service as measured by 30-day readmission rates and lengths of stay.

Design: This is a retrospective observational case-control study with participants matched to themselves.

Setting: UCLA Santa Monica Hospital, a 281-bed academic tertiary care hospital near Los Angeles, California.

Subjects: Patients who had received an EW consultation during the inaugural 20 months of the program (2018–2020), and who had been hospitalized in the prior 2 years from the date of their first EW consult.

Intervention: Inpatient East-West consultation, which may include counseling, acupuncture and/or trigger point injections depending on medical necessity.

Outcome Measures: Thirty-day readmission rates and lengths of hospital admission were compared between the hospitalization that included an EW consult (which included the use of acupuncture and/or trigger point injections when appropriate) and any prior admissions during the 2 years before that EW consult. Secondary outcomes included quantitative analysis of average number of treatments and qualitative assessment of integrative treatment(s) received, conditions treated, and reasons that EW treatment may have been deferred during a consult.

Results: One hundred sixty-five unique patients met the study criteria. The EW consultation was associated with clinically relevant, statistically significant decreased 30-day readmission rates (33.0% vs. 4.6%, $p < 0.001$, odds ratio [OR] 0.10, 95% confidence interval [CI] 0.06–0.17). This effect was similar when limiting the analysis to pain-related admissions (32.3% vs. 3.4%, $p < 0.001$, OR = 0.07, 95% CI 0.03–0.16). Hospital admissions with EW consults were found to have a statistically significant increased length of stay (7.03 days vs. 5.40 days, $p < 0.001$).

Conclusion: The EW medicine, an example of IM, correlates with a reduced risk of 30-day readmission and with modestly increased lengths of stay.

Potdar Swapna. Effectiveness of homoeopathy for the treatment and management of idiopathic granulomatous mastitis in women: A case series. ***Indian Journal of Research in Homoeopathy: 2022;*** **16(1): 41-54p.**

Abstract:

Introduction: Idiopathic Granulomatous Mastitis (IGM) is a rare, debilitating, chronic inflammatory disease of the breast, occurring in women of the child-bearing age, which can clinically, and radiologically mimic abscess, tubercular infection or breast cancer. Homoeopathy can treat the disease by addressing its multifactorial origin, given its holistic approach. The paper presents a case series of 11 patients of IGM treated with classical homoeopathy in place of conventional methods.

Case Summary: After exclusion of differential diagnosis of inflammatory breast lesions by radiology, and biopsy, the patients were given individualised homoeopathic treatment. Common symptoms were pain, single or multiple lumps, abscesses, sinuses, ulcers and discharge in various patients. Descriptive statistics, clinical observation and patient's feedback were used for analysis. 11patients were followed up for a median period of 24 months. All 11 patients experienced subsidence of the lumps with no recurrence and general improvement in health, without any conventional medication or surgical intervention. The initial experience of resolution of IGM with homoeopathic treatment is encouraging. For an evidence-based evaluation of

the results, larger numbers of case studies are required. The key to positive outcome of the case series was meticulous follow up of each patient and intervention with acute homoeopathic remedies, as indicated.

Rao Shalini. Research Highlights. *Indian Journal of Research in Homoeopathy: 2022;* 16(1): 71-73p.

Schulz Steffen, Stritter Wiebke, Gross Marie Michelle, Miltner Dorothea, Rapp Doris, Wilde Britta et al. Quantification of Cardiovascular Regulation Applying Heart Rate Variability Analyses for Different Warm and Moist Chest Compresses in Healthy Subjects. *Journal of Integrative and Complementary Medicine 2022;* 28(3): 268-77p.

Abstract:

Background: In integrative medicine, complementary healing methods, such as external applications (massages, rhythmic rubs, and compresses), are part of the practice and clinical application and have proven their therapeutic effect in various fields.

Objective: Aim of this exploratory, controlled, single-blinded study was to investigate the effects of three different warming chest compresses on cardiovascular regulation by analyzing heart rate variability (HRV) in healthy subjects.

Methods: Over a period of 4 weeks, three different warming chest compresses (a hot water compress, a ginger powder compress, and a mustard flour compress) in 30 healthy subjects were analyzed. For all subjects, 48-h long-term electrocardiograms were recorded, and afterward, epochs of 5 min length extracted and analyzed by different linear and nonlinear HRV indices.

Results: A moist chest compress did not result in any significant short- and long-term stimulation of the autonomic regulation, except for a short-term significant decrease in heart rate (meanNN, $p < 0.05$). Warm and moist chest compresses with ginger flour led to significantly increased HRV (sdNN, $p < 0.05$; symbolic dynamics2, $p < 0.05$) and its complexity (renyi4 entropy, $p < 0.05$) and a significant decrease in heart rate (meanNN, $p < 0.00036$), and thus to a short-term relaxation effect. In contrast, warm and moist chest compresses with mustard flour led to significantly decreased HRV and their complexity (time-, frequency-, and nonlinear dynamics domain, $p < 0.00036$), which can be interpreted as a stress reaction of the autonomous nervous system.

Conclusions: The application of chest compresses led to short-term relaxation effects (ginger) as well as short-term stress effects (mustard) but not to any significant longer-term effect on HRV in healthy subjects.

Schwartz Stephan A. Consciousness, creativity, innovation, and survival. *Explore: 2022;* 18(2): 136-39p.

Thorp KE. Morphogenic fields: A coming of age. *Explore: 2022;* 18(2): 187-94p.

Abstract:

Morphogenesis, the coming-into-being of living organisms, was first described in the 4th century BC by Aristotle, progenitor of biology and embryology. Over the centuries it has been the subject of innumerable commentaries by philosophers, theologians and scientists but no consensus has ever been reached as to its causes. In the late 19th century, along with the emergence of cellular and molecular biology, embryology underwent a renaissance and became a topic of great interest and research. Early on the discipline divided into two opposing factions, those who attempted to explain fetal development on the basis of cellular and molecular mechanisms, and those who invoked the presence of organizing fields. The morphogenic field was first articulated in the early decades of the 20th century by multiple researchers independently of each other. The field became an extremely useful conceptual tool by which to explain a wide range of developmental phenomena. While embryology and genetics originally formed a unified discipline, during the 1930s and 1940s geneticists became progressively skeptical of the field notion. The discovery of the DNA structure by Watson and Crick in the early 1950s decisively settled matters and thereafter the two disciplines pursued different lines of inquiry. After World War II embryology and the field concept went into a decades-long decline. By the 1980s an increasing number of scientists began to critically reexamine the morphogenic field concept and it underwent a second renaissance. In this paper I examine the development and evolution of the field concept, both experimentally and conceptually, and highlight the failure of genetic mechanisms to explain morphogenesis. I provide three instances from the medical literature of developmental phenomena which are only explainable on the basis of morphogenic field dynamics and argue that the field concept must be readmitted into mainstream scientific discourse.

Tremont Geoffrey, Davis Jennifer, Ott Brian R, Uebelacker Lisa, Kenney Lauren, Gillette Tom et al. Feasibility of a Yoga Intervention for Individuals with Mild Cognitive Impairment: A Randomized Controlled Trial. *Journal of Integrative and Complementary Medicine 2022;* 28(3): 250-60p.

Abstract:

Background: Yoga is a potentially low risk intervention for cognitive impairment that combines mental and physical practice and includes instruction on breathing, stress reduction, and mindfulness meditation. Previous research documents that yoga can target modifiable risk factors for mild cognitive impairment (MCI) progression. The authors describe a randomized feasibility trial of yoga for individuals with MCI.

Methods: Participants were 37 individuals with amnestic MCI who were randomly assigned to receive 12 weeks of twice-weekly yoga intervention (YI)

or healthy living education (HLE) classes. Acceptability and feasibility were assessed by tracking adverse events, class attendance, and participant satisfaction. Participants completed neuropsychological and mood measures as well as measures of potential intervention mechanisms at baseline and immediately postintervention.

Results: Participants in both conditions reported high levels of satisfaction and reasonable class attendance rates. Home practice rates were low. There were no adverse events deemed related to the YI. Results showed a medium effect size in favor of the YI in visuospatial skills. The yoga group also showed a large effect size indicating decline in perceived stress compared with the HLE group, whereas HLE resulted in greater reductions in depressive symptoms after the intervention (large effect size).

Conclusions: Study findings indicated that the YI was safe, modestly feasible, and acceptable to older adults with MCI. The authors found preliminary evidence that yoga may improve visuospatial functioning in individuals with MCI. Results support stress reduction as a possible mechanism for the YI. Future studies should address a YI in a larger sample and include strategies to enhance engagement and home practice.

Verma Digvijay, Singh Shilpi, Patel Satish, Singh Manish P. Anatomical characterisation and foliar microscopy of Hypericum perforatum L. ***Indian Journal of Research in Homoeopathy: 2022;*** **16(1): 21-30p.**

Abstract:

Background: Hypericum perforatum L. (family: Hypericaceae), commonly known as St. John's-wort, is a perennial herb and traditionally used for treating anxiety, depression, gastritis, insomnia also menstrual disorders and for healing cuts and burns. In homoeopathy, this remedy is used for the treatment of injuries, tetanus, neuritis, tingling, burning and numbness and constant drowsiness, coccydynia, spasmodic asthmatic attacks with changes of weather, etc.

Objective: The pharmacognostic and fluorescence studies of H. perforatum L. have been conducted to carry out correct identification of plant species for homoeopathic drug preparation and to lay down the standards of the raw drug.

Materials and Methods: The raw drug was supplied by Regional Research Institute of Unani Medicine, Jammu. In the pharmacognostical studies, the macroscopic, microscopic, powder microscopy and fluorescence analysis were performed.

Results: The raw drug was dried, broken and shrivelled pieces of stem, root and leaves. Leaves were pale yellow to brown with prominent blackish-brown dots. The mature stem was circular in shape with two prominent winged projections on both the sides, rays being unibiseriate; pith composed of thin-walled and thick-walled parenchymatous cells with pits. The stomatal index

was 22–25 on lower surface, vein-islet 35–43 and palisade ratio 6–10 recorded.

Conclusion: The presented features along with the powder microscopic, organoleptic characters and fluorescence analysis are diagnostic to establish the standards for ensuring correct identity of the raw drug.

Wayne Peter M, Yeh Gloria Y, Mehta Darshan H. This Is Your Mind: Body on Nature. *Journal of Integrative and Complementary Medicine 2022;* 28(3): 197-201p.

Wright Kathy D, Jones Lenette M, Adams Ingrid Richards, Moss Karen O, Klatt Maryanna D. Co-created health education intervention among older African American women living with hypertension. *Explore: 2022;* 18(2): 234-39p.

Abstract:

Introduction: African Americans over the age of 60 years face disproportionate risk of developing hypertension, which can be mitigated with lifestyle changes. This study examines the acceptability and cost of a patient-centered, co-created health education intervention with older African Americans living with hypertension.

Methods: Twenty women participated in this study that included four weekly, two-hour group sessions centered on hypertension knowledge and calibration of home blood pressure monitors, stress and interpersonal relationship management, sleep and pain management, and healthy eating. The study took place in the Midwest United States.

Results: Descriptive statistics were used to analyze acceptability data that included attendance and a brief investigator-generated questionnaire. Twenty women were enrolled. Sixteen participants attended all four sessions, all reported they intended to continue using the intervention and felt it fit within their culture, routine, and self-care practices. The estimated cost of conducting the intervention was $227.00 (U.S. dollars) per participant.

Conclusions: The co-created health education intervention was acceptable. Given the dire need for cost-effective interventions to improve the adoption of health promoting self-care management behavior, to reduce the prevalence of hypertension in African Americans, the results of this study have implications for future research and practice.

Yang Xingyue, Wang Tianlin, Jiang Yu, Ren Feihong, Jiang Honglin. Patients' Expectancies to Acupuncture: A Systematic Review. *Journal of Integrative and Complementary Medicine 2022;* 28(3): 202-17p.

Abstract:

Objective: This systematic review aimed to document and describe how and when to assess patients' expectancies to acupuncture and the relationship between patients' expectancies and clinical effects.

Materials and Methods: Three English databases, including PubMed, Cochrane Central Register of Controlled Trials, and EMBASE, and four Chinese databases, including the Chinese Biomedicine Literature Database, Chinese Journal Full-text Database, Chinese Scientific Journal Full-text Database, and Wanfang Database, were searched up to February 2020. Studies involving patients' expectancies to acupuncture were included. Based on the detailed situations of patients' expectancies, we made a standardized data extraction table that included the basic information of articles, study design details, and measurement of expectations. Based on the data, a descriptive analysis was performed, covering the characteristics of studies, measuring methods of expectations and the relationship between patients' expectancies and clinical effects. Methodology quality assessment was also performed by the risk of bias and the standards for reporting interventions in controlled trials of acupuncture.

Results: There were 61 randomized controlled trials included in our analysis. The number of articles increased gradually over time and grew significantly after 2008. About half of trials focused on pain alleviation. Expectancies were measured before the treatment ($N = 43$), after the treatment ($N = 3$), and both before and after the treatment ($N = 10$), and five studies did not mention it. The measurement of expectancies used self-made questionnaires or scales ($N = 27$), the Acupuncture Expectations Scale ($N = 6$), and other scales ($N = 11$), while 17 studies did not describe what scale they used. The used questionnaires or scales mostly tried to ascertain the strength of confidence that acupuncture would help. Patients' expectancies and clinical effects were relevant in 19 studies, irrelevant in 21 studies, and were not mentioned in 21 studies.

Conclusions: Patients' expectations to acupuncture have received increasing attention in recent years, but there is still no recognized measurement time and methods. It is critical to develop questions and answers regarding patients' expectations with better discrimination and reliability to accurately assess expectations and to explore the relationship between patients' expectations and acupuncture outcomes in future trials.

Zarabian Kimia, Wannon Avi, Chin May, Kogan Mikhail. Intersection between integrative medicine and neuropathic pain: A case report. *Explore: 2022;* 18(2): 165-69p.

Abstract:

Introduction: Neuropathic pain is a debilitating condition caused by lesion or disease of the somatosensory nervous system. Integrative modalities such as yoga, acupuncture, and massage are evidenced therapies for pain management. Additionally, medical cannabis and cannabinoids are emerging therapies for treatment of neuropathic pain (4,28). The authors of this study report a case of chronic neuropathic pain treated with integrative interventions.

Case Presentation: The patient is a 71-year-old female with a past medical history of chronic neuropathic pain in her lower back and legs, degenerative arthritis, restless leg syndrome, carpal tunnel syndrome, and severe, chronic anxiety, presenting with worsening neuropathic pain. After over a decade of unsuccessful allopathic treatment, the patient sought out a more integrative approach to her pain management. A regimen of acupuncture, massage, gentle yoga, and medical cannabis was recommended. During the COVID-19 pandemic, she was unable to continue most of the integrative modalities and reported a significant increase in pain. The patient then joined a weekly Mind and Body program and began acupuncture treatments again, reporting a steady improvement in pain.

Conclusion: The patient's chronic neuropathic pain was effectively treated using an integrative approach, with a combination of acupuncture, massage, yoga, mind-body approaches, and medical cannabis. While this case originally presented similarly to other cases of chronic neuropathic pain, it is unique in that it demonstrates the importance of an individualized complex approach, highlighting the patient's driven engagement in integrative modalities and medical cannabis.

Allied System of Medicine

Ahsan Saleyha. Seeking accountablity for Ukraine health-care attacks. *Lancet 2022;* 399(10331): 1215-16p.

Angell Blake, Sanuade Olutobi, Adetifa Ifedayo MO, Okeke Iruka N, Abubakar Ibrahim. Population health outcomes in Nigeria compared with other west African countries, 1998–2019: A systematic analysis for the Global Burden of Disease Study. *Lancet 2022;* 399(10330): 1117-29p.

Abstract:

Background: Population-level health and mortality data are crucial for evidence-informed policy but scarce in Nigeria. To fill this gap, we undertook a comprehensive assessment of the burden of disease in Nigeria and compared outcomes to other west African countries.

Methods: In this systematic analysis, using data and results of the Global Burden of Diseases, Injuries, and Risk Factors Study 2019, we analysed patterns of mortality, years of life lost (YLLs), years lived with disability (YLDs), life expectancy, healthy life expectancy (HALE), and health system coverage for Nigeria and 15 other west African countries by gender in 1998 and 2019. Estimates of all-age and age-standardised disability-adjusted life-years for 369 diseases and injuries and 87 risk factors are presented for Nigeria. Health expenditure per person and gross domestic product were extracted from the World Bank repository.

Findings: Between 1998 and 2019, life expectancy and HALE increased in Nigeria by 18% to 64·3 years (95% uncertainty interval [UI] 62·2–66·6), mortality reduced for all age groups for both male and female individuals, and health expenditure per person increased from the 11th to third highest in west Africa by 2018 (US$18·6 in 2001 to $83·75 in 2018). Nonetheless, relative outcomes remained poor; Nigeria ranked sixth in west Africa for age-standardised mortality, seventh for HALE, tenth for YLLs, 12th for health system coverage, and 14th for YLDs in 2019. Malaria (5176·3 YLLs per 100 000 people, 95% UI 2464·0–9591·1) and neonatal disorders (4818·8 YLLs per 100 000, 3865·9–6064·2) were the leading causes of YLLs in Nigeria in 2019. Nigeria had the fourth-highest under-five mortality rate for male individuals (2491·8 deaths per 100 000, 95% UI 1986·1–3140·1) and female individuals (2117·7 deaths per 100 000, 1756·7–2569·1), but among the

lowest mortality for men older than 55 years. There was evidence of a growing non-communicable disease burden facing older Nigerians.

Interpretation: Health outcomes remain poor in Nigeria despite higher expenditure since 2001. Better outcomes in countries with equivalent or lower health expenditure suggest health system strengthening and targeted intervention to address unsafe water sources, poor sanitation, malnutrition, and exposure to air pollution could substantially improve population health.

Funding: The Bill & Melinda Gates Foundation.

Bekker Linda Gail, Garrett Nigel, Goga Ameena, Fairall Lara, Dawson Rodney. Effectiveness of the Ad26.COV2.S vaccine in health-care workers in South Africa (the Sisonke study): Results from a single-arm, open-label, phase 3B, implementation study. *Lancet 2022;* 399(10330): 1141-53p.

Abstract:

Background: We aimed to assess the effectiveness of a single dose of the Ad26.COV2.S vaccine (Johnson & Johnson) in health-care workers in South Africa during two waves of the South African COVID-19 epidemic.

Methods: In the single-arm, open-label, phase 3B implementation Sisonke study, health-care workers aged 18 years and older were invited for vaccination at one of 122 vaccination sites nationally. Participants received a single dose of 5 × 1010 viral particles of the Ad26.COV2.S vaccine. Vaccinated participants were linked with their person-level data from one of two national medical insurance schemes (scheme A and scheme B) and matched for COVID-19 risk with an unvaccinated member of the general population. The primary outcome was vaccine effectiveness against severe COVID-19, defined as COVID-19-related admission to hospital, hospitalisation requiring critical or intensive care, or death, in health-care workers compared with the general population, ascertained 28 days or more after vaccination or matching, up to data cutoff. This study is registered with the South African National Clinical Trial Registry, DOH-27-022021-6844, ClinicalTrials.gov, NCT04838795, and the Pan African Clinical Trials Registry, PACTR202102855526180, and is closed to accrual.

Findings: Between Feb 17 and May 17, 2021, 477 102 health-care workers were enrolled and vaccinated, of whom 357 401 (74·9%) were female and 119 701 (25·1%) were male, with a median age of 42·0 years (33·0–51·0).

215 813 vaccinated individuals were matched with 215 813 unvaccinated individuals. As of data cutoff (July 17, 2021), vaccine effectiveness derived from the total matched cohort was 83% (95% CI 75–89) to prevent COVID-19-related deaths, 75% (69–82) to prevent COVID-19-related hospital admissions requiring critical or intensive care, and 67% (62–71) to prevent COVID-19-related hospitalisations. The vaccine effectiveness for all three outcomes were consistent across scheme A and scheme B. The vaccine effectiveness was maintained in older health-care workers and those with comorbidities including HIV infection. During the course of the study, the beta (B.1.351) and then the delta (B.1.617.2) SARS-CoV-2 variants of concerns were dominant, and vaccine effectiveness remained consistent (for scheme A plus B vaccine effectiveness against COVID-19-related hospital admission during beta wave was 62% [95% CI 42–76] and during delta wave was 67% [62–71], and vaccine effectiveness against COVID-19-related death during beta wave was 86% [57–100] and during delta wave was 82% [74–89]).

Interpretation: The single-dose Ad26.COV2.S vaccine shows effectiveness against severe COVID-19 disease and COVID-19-related death after vaccination, and against both beta and delta variants, providing real-world evidence for its use globally.

Funding: National Treasury of South Africa, the National Department of Health, Solidarity Response Fund NPC, The Michael & Susan Dell Foundation, The Elma Vaccines and Immunization Foundation, and the Bill & Melinda Gates Foundation.

Booth Amy. Activists welcome Colombia's decriminalisation of abortion. *Lancet 2022;* 399(10328): 899p.

Craig Timothy, Magerl Markus, Levy Donald S, Reshef Avner, Doyle Mittie K. Prophylactic use of an anti-activated factor XII monoclonal antibody, garadacimab, for patients with C1-esterase inhibitor-deficient hereditary angioedema: A randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet 2022;* 399(10328): 945-55p.

Abstract:

Background: Hereditary angioedema is associated with dysregulation of the kallikrein–kinin system. Factor XII (FXII) is a key initiator of the kallikrein–kinin system, which produces bradykinin, a central mediator of angioedema. Garadacimab (CSL Behring) is a first-in-class, fully human, immunoglobulin G4 monoclonal antibody targeting activated FXII, intended

to prevent attacks in patients with C1-esterase inhibitor-deficient hereditary angioedema (HAE-C1-INH). We aimed to investigate garadacimab as a treatment every 4 weeks for patients with HAE-C1-INH.

Methods: In this double-blind, placebo-controlled, phase 2 study, patients with HAE-C1-INH were recruited from 12 research centres in Canada, Germany, Israel, and the USA. Eligible patients were aged 18–65 years and must have had at least four attacks of any severity over a consecutive 2-month period during the 3 months before screening or initiation of previous hereditary angioedema prophylaxis. After a run-in period of 4–8 weeks, patients were randomly assigned (1:1:1:1), using an interactive response technology via block randomisation (block sizes of 1–4), to either placebo or 75 mg, 200 mg, or 600 mg garadacimab. Patients were given an initial intravenous loading dose, and then, on day 6 and every 4 weeks for 12 weeks, they were given a subcutaneous dose of their allocated treatment. The primary endpoint was the number of monthly attacks in the intention-to-treat population (defined as all patients who underwent screening, provided consent, and were assigned to treatment) during the 12-week subcutaneous administration period assessed in the 200 mg and 600 mg garadacimab groups versus placebo. Safety was assessed in all patients who received at least one dose or partial dose of study treatment. This study is registered with ClinicalTrials.gov, NCT03712228.

Findings: Between Oct 29, 2018, and Aug 28, 2019, 54 patients were screened, of whom 32 were randomly assigned to either placebo (n=8) or 75 mg (n=9), 200 mg (n=8), or 600 mg (n=7) garadacimab. The median age was 39·5 years (28·0–52·5) and 18 (56%) of 32 patients were female and 14 (34%) were male. The median number of monthly attacks during the 12-week subcutaneous treatment period was 4·6 (IQR 3·1–5·0) with placebo, 0·0 (0·0–0·4) with 75 mg garadacimab, 0·0 (0·0–0·0) with 200 mg garadacimab, and 0·3 (0·0–0·7) with 600 mg garadacimab. Compared with placebo, the rate of attacks was significantly reduced with garadacimab at 200 mg (reduced by 100% [95% CI 98–101]; p=0·0002) and 600 mg (reduced by 93% [54–110]; p=0·0003). No serious adverse events, deaths, or adverse events of special interest (anaphylaxis, thromboembolic events, and bleeding events) were observed.

Interpretation: Garadacimab 200 mg and 600 mg every 4 weeks significantly reduced the number of monthly attacks versus placebo and was well tolerated during the study. Garadacimab is an efficacious, subcutaneous prophylaxis in patients with HAE-C1-INH and warrants phase 3 evaluation.

Funding: CSL Behring.

Drivenes Jakob Lillemoen, Betz Regina C, Bygum Anette. Girl with unruly locks: Molecular genetics makes a diagnosis of uncombable hair syndrome. *Lancet 2022;* 399(10329): 1079p.

Edqvist Malin, Dahlen Hannah G, Haggsgard Cecilia, Tern Helena, Rubertsson Christine. Effect of two midwives during the second stage of labour to reduce severe perineal trauma (Oneplus): A multicentre, randomised controlled trial in Sweden. *Lancet 2022;* 399(10331): 1242-53p.

Abstract:

Background: Severe perineal trauma (SPT) affecting the anal sphincter muscle complex is a serious complication following childbirth, associated with short-term and long-term maternal morbidity. Effective preventive strategies are still scarce. The aim of the Oneplus trial was to test the hypothesis that the presence of a second midwife during the second stage of labour, with the purpose of preventing SPT, would result in fewer injuries affecting the anal sphincter than if attended by one midwife.

Methods: In this multicentre, randomised, controlled parallel group, unmasked trial done at five obstetric units in Sweden, women were randomly assigned to be assisted by either one or two midwives in late second stage. Nulliparous women and women planning the first vaginal birth after caesarean section who were age 18–47 years were randomly assigned to an intervention when reaching the second stage of labour. Further inclusion criteria were gestational week 37+0, carrying a singleton live fetus in vertex presentation, and proficiency in either Swedish, English, Arabic, or Farsi. Exclusion criteria were a multiple pregnancy, intrauterine fetal demise, a planned caesarean section, or women who were less than 37 weeks pregnant. Randomisation to the intervention group of two midwives or standard care group of one midwife (1:1) was done using a computer-based program and treatment groups were allocated by use of sealed opaque envelopes. All women and midwives were aware of the group assignment, but the statistician from Clinical Studies Forum South, who did the analyses, was masked to group assignment. Midwives were instructed to implement existing prevention models and the second midwife was to assist on instruction of the primary midwife, when asked. Midwives were also instructed to complete case report forms detailing assistance techniques and perineal trauma prevention techniques. The primary outcome was the proportion of women who had SPT, for which odds ratios (ORs) and 95% CIs

were calculated, and logistic regression was done to adjust for study site. All analyses were done according to intention to treat. The trial is registered with ClinicalTrials.gov, NCT0377096.

Findings: Between Dec 10, 2018, and March 21, 2020, 8866 women were assessed for eligibility, and 4264 met the inclusion criteria and agreed to participate. 3776 (88·5%) of 4264 women were randomly assigned to an intervention after reaching the second stage of labour. 1892 women were assigned to collegial assistance (two midwives) during the second stage of labour and 1884 women were assigned to standard care (one midwife). 13 women in each group did not meet the inclusion criteria and were excluded. After further exclusions, 1546 women spontaneously gave birth in the intervention group and 1513 in the standard care group. 1546 women in the intervention group and 1513 in the standard care group were included in the intention-to-treat analysis of the primary outcome. There was a significant reduction in SPT in the intervention group (3·9% [61 of 1546] vs 5·7% [86 of 1513]; adjusted OR 0·69 (0·49–0·97).

Interpretation: The presence of two midwives during the active second stage can reduce SPT in women giving birth for the first time.

Funding: The Swedish Research Council for Health, Working Life and Welfare; Jan Hains Research Foundation; and Skane County Council's Research and Development Foundation.

Ensuring care for people with depression. *Lancet 2022;* 399(10328): 885p.

Feikin Daniel R, Higdon Melissa M, Abu Raddad Laith J, Andrews Nick, Patel Minal K. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: Results of a systematic review and meta-regression. *Lancet 2022;* 399(10328): 924-44p.

Abstract:

Background: Knowing whether COVID-19 vaccine effectiveness wanes is crucial for informing vaccine policy, such as the need for and timing of booster doses. We aimed to systematically review the evidence for the duration of protection of COVID-19 vaccines against various clinical outcomes, and to assess changes in the rates of breakthrough infection caused by the delta variant with increasing time since vaccination.

Methods: This study was designed as a systematic review and meta-regression. We did a systematic review of preprint and peer-reviewed published article databases from June 17, 2021, to Dec 2, 2021. Randomised controlled trials of COVID-19 vaccine efficacy and observational studies of COVID-19 vaccine effectiveness were eligible. Studies with vaccine efficacy or effectiveness estimates at discrete time intervals of people who had received full vaccination and that met predefined screening criteria underwent full-text review. We used random-effects meta-regression to estimate the average change in vaccine efficacy or effectiveness 1–6 months after full vaccination.

Findings: Of 13 744 studies screened, 310 underwent full-text review, and 18 studies were included (all studies were carried out before the omicron variant began to circulate widely). Risk of bias, established using the risk of bias 2 tool for randomised controlled trials or the risk of bias in non-randomised studies of interventions tool was low for three studies, moderate for eight studies, and serious for seven studies. We included 78 vaccine-specific vaccine efficacy or effectiveness evaluations (Pfizer–BioNTech-Comirnaty, n=38; Moderna-mRNA-1273, n=23; Janssen-Ad26.COV2.S, n=9; and AstraZeneca-Vaxzevria, n=8). On average, vaccine efficacy or effectiveness against SARS-CoV-2 infection decreased from 1 month to 6 months after full vaccination by 21·0 percentage points (95% CI 13·9–29·8) among people of all ages and 20·7 percentage points (10·2–36·6) among older people (as defined by each study, who were at least 50 years old). For symptomatic COVID-19 disease, vaccine efficacy or effectiveness decreased by 24·9 percentage points (95% CI 13·4–41·6) in people of all ages and 32·0 percentage points (11·0–69·0) in older people. For severe COVID-19 disease, vaccine efficacy or effectiveness decreased by 10·0 percentage points (95% CI 6·1–15·4) in people of all ages and 9·5 percentage points (5·7–14·6) in older people. Most (81%) vaccine efficacy or effectiveness estimates against severe disease remained greater than 70% over time.

Interpretation: COVID-19 vaccine efficacy or effectiveness against severe disease remained high, although it did decrease somewhat by 6 months after full vaccination. By contrast, vaccine efficacy or effectiveness against infection and symptomatic disease decreased approximately 20–30 percentage points by 6 months. The decrease in vaccine efficacy or effectiveness is likely caused by, at least in part, waning immunity, although an effect of bias cannot be ruled out. Evaluating vaccine efficacy or effectiveness beyond 6 months will be crucial for updating COVID-19 vaccine policy.

Funding: Coalition for Epidemic Preparedness Innovations.

Fendler Annika, Shepherd Scott TC, Au Lewis, Wu Mary, Turajlic Samra. Omicron neutralising antibodies after third COVID-19 vaccine dose in patients with cancer. *Lancet 2022;* 399(10328): 905-07p.

Grubbs Vanessa, Cerdena Jessica P, Non Amy L. Misuse of race in the search for disease-causing alleles. *Lancet 2022;* 399(10330): 1110-1111p.

Habibzadeh Farrokh. Disparity in the selection of patients in clinical trials. *Lancet 2022;* 399(10329): 1048p.

Hassan Razeen, Meng Leow Voon, Ngee Kee Thian, I-Vern Lim, Subramaniam Manisekar. Extraskeletal Ewing sarcoma of the duodenum presenting as duodenojejunal intussusception. *Lancet 2022;* 399(10331): 1265p.

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McDonald Craig M, Marban Eduardo, Hendrix Suzanne, Hogan Nathaniel, Rogers Russell G. Repeated intravenous cardiosphere-derived cell therapy in late-stage Duchenne muscular dystrophy (HOPE-2): A multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet 2022;* 399(10329): 1049-58p.

Abstract:

Background: Cardiosphere-derived cells (CDCs) ameliorate skeletal and cardiac muscle deterioration in experimental models of Duchenne muscular

dystrophy. The HOPE-2 trial examined the safety and efficacy of sequential intravenous infusions of human allogeneic CDCs in late-stage Duchenne muscular dystrophy.

Methods: In this multicentre, randomised, double-blind, placebo-controlled, phase 2 trial, patients with Duchenne muscular dystrophy, aged 10 years or older with moderate upper limb impairment, were enrolled at seven centres in the USA. Patients were randomly assigned (1:1) using stratified permuted blocks to receive CAP-1002 (1·5 × 108 CDCs) or placebo intravenously every 3 months for a total of four infusions. Clinicians, caregivers, patients, and clinical operations personnel were fully masked to treatment groups. The primary outcome was the change in mid-level elbow Performance of Upper Limb version 1.2 (PUL 1.2) score at 12 months, assessed in the intention-to-treat population. Safety was assessed in all individuals who received an investigational product. This trial is registered with ClinicalTrials.gov, NCT03406780.

Findings: Between March 1, 2018, and March 31, 2020, 26 male patients with Duchenne muscular dystrophy were enrolled, of whom eight were randomly assigned to the CAP-1002 group and 12 to the placebo group (six were not randomised due to screening failure). In patients who had a post-treatment PUL 1.2 assessment (eight in the CAP-1002 group and 11 in the placebo group), the mean 12-month change from baseline in mid-level elbow PUL1.2 favoured CAP-1002 over placebo (percentile difference 36·2, 95% CI 12·7–59·7; difference of 2·6 points; p=0·014). Infusion-related hypersensitivity reactions without long-term sequelae were observed in three patients, with one patient discontinuing therapy due to a severe allergic reaction. No other major adverse reactions were noted, and no deaths occurred.

Interpretation: CAP-1002 cell therapy appears to be safe and effective in reducing deterioration of upper limb function in patients with late-stage Duchenne muscular dystrophy. Various measures of cardiac function and structure were also improved in the CAP-1002 group compared with the placebo group. Longer-term extension studies are needed to confirm the therapeutic durability and safety of CAP-1002 beyond 12 months for the treatment of skeletal myopathy and cardiomyopathy in Duchenne muscular dystrophy.

Funding: Capricor Therapeutics.

McGarvey Lorcan P, Birring Surinder S, Morice Alyn H, Dicpinigaitis Peter V, Smith Jaclyn A. Efficacy and safety of gefapixant, a P2X3

receptor antagonist, in refractory chronic cough and unexplained chronic cough (COUGH-1 and COUGH-2): Results from two double-blind, randomised, parallel-group, placebo-controlled, phase 3 trials. ***Lancet 2022;*** **399(10328): 909-23p.**

Abstract:

Background: Gefapixant is an oral P2X3 receptor antagonist that has previously shown efficacy and safety in refractory chronic cough and unexplained chronic cough. We therefore aim to confirm the efficacy and safety of gefapixant in participants with refractory chronic cough and unexplained chronic cough.

Methods: COUGH-1 and COUGH-2 were both double-blind, randomised, parallel-group, placebo-controlled, phase 3 trials. COUGH-1 was done in 156 sites in 17 countries and COUGH-2 in 175 sites in 20 countries. We enrolled participants who were 18 years or older with a diagnosis of refractory chronic cough or unexplained chronic cough of 1 year duration or more. Participants were also required to have a cough severity visual analogue scale score of 40 mm or more at screening and baseline. Eligible participants were randomly allocated (1:1:1), using a computer-generated allocation schedule, to one of three treatment groups: placebo, gefapixant 15 mg twice per day, or gefapixant 45 mg twice per day. All study treatments were given orally. Participants were treated over a 12-week main study period in COUGH-1 and a 24-week main study period in COUGH-2; followed by extension periods for a total of up to 52 weeks of treatment in both trials. The primary outcome was placebo-adjusted mean change in 24-h cough frequency at 12 weeks in COUGH-1 and 24 weeks in COUGH-2. Both studies were registered with ClinicalTrials.gov, NCT03449134 (COUGH-1) and NCT03449147 (COUGH-2).

Findings: From March 14, 2018, (first participant screened) to July 26, 2019, (last participant screened) 732 patients were recruited in COUGH-1 and 1317 in COUGH-2. COUGH-1 randomly assigned and treated 730 participants (243 [33×3%] with placebo, 244 [33×4%] with gefapixant 15 mg twice per day, and 243 [33×3%] with gefapixant 45 mg twice per day); COUGH-2 randomly assigned and treated 1314 participants (435 [33×1%] with placebo, 440 [33×5%] with gefapixant 15 mg twice per day, and 439 [33×4%] with gefapixant 45 mg twice per day). Participants were mostly female (542 [74×2%] of 730 in COUGH-1 and 984 [74×9%] of 1314 in COUGH-2). The mean age was 59×0 years (SD 12×6) in COUGH-1 and 58×1 years (12×1) in COUGH-2, and the mean cough duration was 11·6 years (SD 9·5) in COUGH-1 and 11·2 years (9·8) in COUGH-2. Gefapixant 45 mg twice

per day showed significant reductions in 24-h cough frequency compared with placebo at week 12 in COUGH-1 (18·5% [95% CI 32·9–0·9]; p=0·041) and at week 24 in COUGH-2 (14·6% [26·1–1·4]; p=0·031). Gefapixant 15 mg twice per day did not show a significant reduction in cough frequency versus placebo in both studies. The most common adverse events were related to taste disturbance: ageusia (36 [4·9%] of 730 in COUGH-1 and 86 [6·5%] of 1314 in COUGH-2), dysgeusia (118 [16·2%] in COUGH-1 and 277 [21·1%] in COUGH-2), hypergeusia (3 [0·4%] in COUGH-1 and 6 [0×5%] in COUGH-2), hypogeusia (19 [2·6%] in COUGH-1 and 80 [6·1%] in COUGH-2), and taste disorder (28 [3·8%] in COUGH-1 and 46 [3·5%] in COUGH-2).

Interpretation: Gefapixant 45 mg twice per day is the first treatment to show efficacy with an acceptable safety profile in phase 3 clinical trials for refractory chronic cough or unexplained chronic cough.

Funding: Merck Sharp & Dohme.

Mosha Jacklin F, Kulkarni Manisha A, Lukole Eliud, Matowo Nancy S, Protopopoff Natacha. Effectiveness and cost-effectiveness against malaria of three types of dual-active-ingredient long-lasting insecticidal nets (LLINs) compared with pyrethroid-only LLINs in Tanzania: A four-arm, cluster- randomised trial. *Lancet 2022;* 399(10331): 1227-41p.

Abstract:

Background: Long-lasting insecticidal nets (LLINs) have successfully reduced malaria in sub-Saharan Africa, but their effectiveness is now partly compromised by widespread resistance to insecticides among vectors. We evaluated new classes of LLINs with two active ingredients with differing modes of action against resistant malaria vectors.

Methods: We did a four-arm, cluster-randomised trial in Misungwi, Tanzania. Clusters were villages, or groups of hamlets, with at least 119 households containing children aged 6 months to 14 years living in the cluster's core area. Constrained randomisation was used to allocate clusters (1:1:1:1) to receive one of four types of LLIN treated with the following: α-cypermethrin only (pyrethroid-only [reference] group); pyriproxyfen and α-cypermethrin (pyriproxyfen group); chlorfenapyr and α-cypermethrin (chlorfenapyr group); or the synergist piperonyl butoxide and permethrin (piperonyl butoxide group). At least one LLIN was distributed for every two people. Community members and the field team were masked to group allocation. Malaria prevalence data were collected through cross-sectional

surveys of randomly selected households from each cluster, in which children aged 6 months to 14 years were assessed for Plasmodium falciparum malaria infection by rapid diagnostic tests. The primary outcome was malaria infection prevalence at 24 months after LLIN distribution, comparing each of the dual-active-ingredient LLINs to the standard pyrethroid-only LLINs in the intention-to-treat population. The primary economic outcome was cost-effectiveness of dual-active-ingredient LLINs, based on incremental cost per disability-adjusted life-year (DALY) averted compared with pyrethroid-only LLINs, modelled over a 2-year period; we included costs of net procurement and malaria diagnosis and treatment, and estimated DALYs in all age groups. This study is registered with ClinicalTrials.gov (NCT03554616), and is ongoing but no longer recruiting.

Findings: 84 clusters comprising 39 307 households were included in the study between May 11 and July 2, 2018. 147 230 LLINs were distributed among households between Jan 26 and Jan 28, 2019. Use of study LLINs was reported in 3155 (72·1%) of 4378 participants surveyed at 3 months post-distribution and decreased to 8694 (40·9%) of 21 246 at 24 months, with varying rates of decline between groups. Malaria infection prevalence at 24 months was 549 (45·8%) of 1199 children in the pyrethroid-only reference group, 472 (37·5%) of 1258 in the pyriproxyfen group (adjusted odds ratio 0·79 [95% CI 0·54–1·17], p=0·2354), 512 (40·7%) of 1259 in the piperonyl butoxide group (0·99 [0·67–1·45], p=0·9607), and 326 [25·6%] of 1272 in the chlorfenapyr group (0·45 [0·30–0·67], p=0·0001). Skin irritation or paraesthesia was the most commonly reported side-effect in all groups. Chlorfenapyr LLINs were the most cost-effective LLINs, costing only US$19 (95% uncertainty interval 1–105) more to public providers or $28 (11–120) more to donors per DALY averted over a 2-year period compared with pyrethroid-only LLINs, and saving costs from societal and household perspectives.

Interpretation: After 2 years, chlorfenapyr LLINs provided significantly better protection than pyrethroid-only LLINs against malaria in an area with pyrethroid-resistant mosquitoes, and the additional cost of these nets would be considerably below plausible cost-effectiveness thresholds ($292–393 per DALY averted). Before scale-up of chlorfenapyr LLINs, resistance management strategies are needed to preserve their effectiveness. Poor textile and active ingredient durability in the piperonyl butoxide and pyriproxyfen LLINs might have contributed to their relative lack of effectiveness compared with standard LLINs.

Funding: Joint Global Health Trials scheme (UK Foreign, Commonwealth and Development Office; UK Medical Research Council; Wellcome; UK

Department of Health and Social Care), US Agency for International Development, President's Malaria Initiative.

NCD Countdown 2030: Efficient pathways and strategic investments to accelerate progress towards the Sustainable Development Goal target 3.4 in low-income and middle-income countries. *Lancet 2022;* 399(10331): 1266-78p.

Abstract:

Most countries have made little progress in achieving the Sustainable Development Goal (SDG) target 3.4, which calls for a reduction in premature mortality from non-communicable diseases (NCDs) by a third from 2015 to 2030. In this Health Policy paper, we synthesise the evidence related to interventions that can reduce premature mortality from the major NCDs over the next decade and that are feasible to implement in countries at all levels of income. Our recommendations are intended as generic guidance to help 123 low-income and middle-income countries meet SDG target 3.4; country-level applications require additional analyses and consideration of the local implementation and utilisation context. Protecting current investments and scaling up these interventions is especially crucial in the context of COVID-19-related health system disruptions. We show how cost-effectiveness data and other information can be used to define locally tailored packages of interventions to accelerate rates of decline in NCD mortality. Under realistic implementation constraints, most countries could achieve (or almost achieve) the NCD target using a combination of these interventions; the greatest gains would be for cardiovascular disease mortality. Implementing the most efficient package of interventions in each world region would require, on average, an additional US$18 billion annually over 2023–30; this investment could avert 39 million deaths and generate an average net economic benefit of $2·7 trillion, or $390 per capita. Although specific clinical intervention pathways would vary across countries and regions, policies to reduce behavioural risks, such as tobacco smoking, harmful use of alcohol, and excess sodium intake, would be relevant in nearly every country, accounting for nearly two-thirds of the health gains of any locally tailored NCD package. By 2030, ministries of health would need to contribute about 20% of their budgets to high-priority NCD interventions. Our report concludes with a discussion of financing and health system implementation considerations and reflections on the NCD agenda beyond the SDG target 3.4 and beyond the SDG period.

Non-communicable diseases: What now? *Lancet 2022;* 399(10331): 1201p.

Rearte Analia, Castelli Juan Manuel, Rearte Ramiro, Fuentes Nora, Vizzotti Carla. Effectiveness of rAd26-rAd5, ChAdOx1 nCoV-19, and BBIBP-CorV vaccines for risk of infection with SARS-CoV-2 and death due to COVID-19 in people older than 60 years in Argentina: A test-negative, case-control, and retrospective longitudinal study. *Lancet 2022;* 399(10331): 1254-64p.

Abstract:

Background: In January, 2021, a vaccination campaign against COVID-19 was initiated with the rAd26-rAd5, ChAdOx1 nCoV-19, and BBIBP-CorV vaccines in Argentina. The objective of this study was to estimate vaccine effectiveness at reducing risk of SARS-CoV-2 infection and COVID-19 deaths in people older than 60 years.

Methods: In this test-negative, case-control, and retrospective longitudinal study done in Argentina, we evaluated the effectiveness of three vaccines (rAd26-rAd5, ChAdOx1 nCoV-19, and BBIBP-CorV) on SARS-CoV-2 infection and risk of death in people with RT-PCR confirmed COVID-19, using data from the National Surveillance System (SNVS 2.0). All individuals aged 60 years or older reported to SNVS 2.0 as being suspected to have COVID-19 who had disease status confirmed with RT-PCR were included in the study. Unvaccinated individuals could participate in any of the analyses. People with suspected COVID-19 who developed symptoms before the start of the implementation of the vaccination programme for their age group or district were excluded from the study. The odds ratio of SARS-CoV-2 infection was evaluated by logistic regression and the risk of death in individuals with RT-PCR confirmed COVID-19 was evaluated by proportional hazard regression models, adjusted for possible confounders: age at the time of the symptom onset date, sex, district of residence, epidemiological week corresponding to the symptom onset date, and history of COVID-19. The estimation of vaccine effectiveness to prevent death due to COVID-19 was done indirectly by combining infection and death estimates. In addition, we evaluated the effect of the first dose of viral vector vaccines across time.

Findings: From Jan 31, to Sept 14, 2021, 1 282 928 individuals were included, of whom 687 167 (53·6%) were in the rAd26-rAd5 analysis, 358 431 (27·6%) in the ChAdOx1 nCoV-19 analysis, and 237 330 (18·5%) in the BBIBP-CorV analysis. Vaccine effectiveness after two doses was high for all three vaccines, adjusted odds ratio 0·36 (95% CI 0·35–0·37) for rAd26-rAd5, 0·32 (0·31–0·33) for ChAdOx1 nCoV-19, and 0·56 (0·55–0·58) for BBIBP-CorV. After two doses, the effect on deaths was higher than that on

risk of infection: adjusted hazard ratio 0·19 (95% CI 0·18–0·21) for rAd26-rAd5, 0·20 (0·18–0·22) for ChAdOx1 nCoV-19, and 0·27 (0·25–0·29) for BBIBP-CorV. The indirectly estimated effectiveness on deaths was 93·1% (95% CI 92·6–93·5) for rAd26-rAd5, 93·7% (93·2–94·3) for ChAdOx1 nCoV-19, and 85·0% (84·0–86·0) for BBIBP-CorV following two doses. First dose effect of viral vector vaccines remained stable over time.

Interpretation: The vaccines used in Argentina showed effectiveness in reducing infection and death by SARS-CoV-2 and COVID-19.

Funding: None.

Reid Ian R, Billington Emma O. Drug therapy for osteoporosis in older adults. *Lancet 2022;* 399(10329): 1080-92p.

Abstract:

The goal of osteoporosis management is to prevent fractures. Several pharmacological agents are available to lower fracture risk, either by reducing bone resorption or by stimulating bone formation. Bisphosphonates are the most widely used anti-resorptives, reducing bone turnover markers to low premenopausal concentrations and reducing fracture rates (vertebral by 50–70%, non-vertebral by 20–30%, and hip by ~40%). Bisphosphonates bind avidly to bone mineral and have an offset of effect measured in months to years. Long term, continuous use of oral bisphosphonates is usually interspersed with drug holidays of 1–2 years, to minimise the risk of atypical femoral fractures. Denosumab is a monoclonal antibody against RANKL that potently inhibits osteoclast development and activity. Denosumab is administered by subcutaneous injection every 6 months. Anti-fracture effects of denosumab are similar to those of the bisphosphonates, but there is a pronounced loss of anti-resorptive effect from 7 months after the last injection, which can result in clusters of rebound vertebral fractures. Two classes of anabolic drugs are now available to stimulate bone formation. Teriparatide and abaloparatide both target the parathyroid hormone-1 receptor, and are given by daily subcutaneous injection for up to 2 years. Romosozumab is an anti-sclerostin monoclonal antibody that stimulates bone formation and inhibits resorption. Romosozumab is given as monthly subcutaneous injections for 1 year. Head-to-head studies suggest that anabolic agents have greater anti-fracture efficacy and produce larger increases in bone density than anti-resorptive drugs. The effects of anabolic agents are transient, so transition to anti-resorptive drugs is required. The optimal strategy for cycling

anabolics, anti-resorptives, and off-treatment periods remains to be determined.

Shah Sanjiv J, Borlaug Barry A, Chung Eugene S, Cutlip Donald E, Zirlik Andreas. Atrial shunt device for heart failure with preserved and mildly reduced ejection fraction (REDUCE LAP-HF II): A randomised, multicentre, blinded, sham-controlled trial. ***Lancet 2022;*** **399(10330): 1130-40p.**

Abstract:

Background: Placement of an interatrial shunt device reduces pulmonary capillary wedge pressure during exercise in patients with heart failure and preserved or mildly reduced ejection fraction. We aimed to investigate whether an interatrial shunt can reduce heart failure events or improve health status in these patients.

Methods: In this randomised, international, blinded, sham-controlled trial performed at 89 health-care centres, we included patients (aged ≥40 years) with symptomatic heart failure, an ejection fraction of at least 40%, and pulmonary capillary wedge pressure during exercise of at least 25 mm Hg while exceeding right atrial pressure by at least 5 mm Hg. Patients were randomly assigned (1:1) to receive either a shunt device or sham procedure. Patients and outcome assessors were masked to randomisation. The primary endpoint was a hierarchical composite of cardiovascular death or non-fatal ischemic stroke at 12 months, rate of total heart failure events up to 24 months, and change in Kansas City Cardiomyopathy Questionnaire overall summary score at 12 months. Pre-specified subgroup analyses were conducted for the heart failure event endpoint. Analysis of the primary endpoint, all other efficacy endpoints, and safety endpoints was conducted in the modified intention-to-treat population, defined as all patients randomly allocated to receive treatment, excluding those found to be ineligible after randomisation and therefore not treated. This study is registered with ClinicalTrials.gov, NCT03088033.

Findings: Between May 25, 2017, and July 24, 2020, 1072 participants were enrolled, of whom 626 were randomly assigned to either the atrial shunt device (n=314) or sham procedure (n=312). There were no differences between groups in the primary composite endpoint (win ratio 1·0 [95% CI 0·8–1·2]; p=0·85) or in the individual components of the primary endpoint. The prespecified subgroups demonstrating a differential effect of atrial shunt device treatment on heart failure events were pulmonary artery systolic pressure at 20W of exercise (pinteraction=0·002 [>70 mm Hg

associated with worse outcomes]), right atrial volume index (pinteraction=0·012 [≥29·7 mL/m2, worse outcomes]), and sex (pinteraction=0·02 [men, worse outcomes]). There were no differences in the composite safety endpoint between the two groups (n=116 [38%] for shunt device vs n=97 [31%] for sham procedure; p=0·11).

Interpretation: Placement of an atrial shunt device did not reduce the total rate of heart failure events or improve health status in the overall population of patients with heart failure and ejection fraction of greater than or equal to 40%.

Funding: Corvia Medical.

Steen Wouter van der, Graaf Rob A van de, Chalos Vicky, Lingsma Hester F, Roozenbeek Bob. Safety and efficacy of aspirin, unfractionated heparin, both, or neither during endovascular stroke treatment (MR CLEAN-MED): An open-label, multicentre, randomised controlled trial. *Lancet 2022;* 399(10329): 1059-69p.

Abstract:

Background: Aspirin and unfractionated heparin are often used during endovascular stroke treatment to improve reperfusion and outcomes. However, the effects and risks of anti-thrombotics for this indication are unknown. We therefore aimed to assess the safety and efficacy of intravenous aspirin, unfractionated heparin, both, or neither started during endovascular treatment in patients with ischaemic stroke.

Methods: We did an open-label, multicentre, randomised controlled trial with a 2 × 3 factorial design in 15 centres in the Netherlands. We enrolled adult patients (ie, ≥18 years) with ischaemic stroke due to an intracranial large-vessel occlusion in the anterior circulation in whom endovascular treatment could be initiated within 6 h of symptom onset. Eligible patients had a score of 2 or more on the National Institutes of Health Stroke Scale, and a CT or MRI ruling out intracranial haemorrhage. Randomisation was done using a web-based procedure with permuted blocks and stratified by centre. Patients were randomly assigned (1:1) to receive either periprocedural intravenous aspirin (300 mg bolus) or no aspirin, and randomly assigned (1:1:1) to receive moderate-dose unfractionated heparin (5000 IU bolus followed by 1250 IU/h for 6 h), low-dose unfractionated heparin (5000 IU bolus followed by 500 IU/h for 6 h), or no unfractionated heparin. The primary outcome was the score on the modified Rankin Scale at 90 days. Symptomatic intracranial haemorrhage was the main safety

outcome. Analyses were based on intention to treat, and treatment effects were expressed as odds ratios (ORs) or common ORs, with adjustment for baseline prognostic factors. This trial is registered with the International Standard Randomised Controlled Trial Number, ISRCTN76741621.

Findings: Between Jan 22, 2018, and Jan 27, 2021, we randomly assigned 663 patients; of whom, 628 (95%) provided deferred consent or died before consent could be asked and were included in the modified intention-to-treat population. On Feb 4, 2021, after unblinding and analysis of the data, the trial steering committee permanently stopped patient recruitment and the trial was stopped for safety concerns. The risk of symptomatic intracranial haemorrhage was higher in patients allocated to receive aspirin than in those not receiving aspirin (43 [14%] of 310 vs 23 [7%] of 318; adjusted OR 1·95 [95% CI 1·13–3·35]) as well as in patients allocated to receive unfractionated heparin than in those not receiving unfractionated heparin (44 [13%] of 332 vs 22 [7%] of 296; 1·98 [1·14–3·46]). Both aspirin (adjusted common OR 0·91 [95% CI 0·69–1·21]) and unfractionated heparin (0·81 [0·61–1·08]) led to a non-significant shift towards worse modified Rankin Scale scores.

Interpretation: Periprocedural intravenous aspirin and unfractionated heparin during endovascular stroke treatment are both associated with an increased risk of symptomatic intracranial haemorrhage without evidence for a beneficial effect on functional outcome.

Funding: The Collaboration for New Treatments of Acute Stroke consortium, the Brain Foundation Netherlands, the Ministry of Economic Affairs, Stryker, Medtronic, Cerenovus, and the Dutch Heart Foundation.

Theng Elizabeth H, Weinstein Lee S, Collins Michael T. Calvarial hyperostosis in primary hyperparathyroidism and other settings of increased cAMP signalling. *Lancet 2022;* 399(10328): 956p.
Webster Paul. Report finds no common cause for mystery brain disease. *Lancet 2022;* 399(10329): 1035-36p.

Yakovenko Victoria, Brauner Ron, Votinov Ekaterina, Goldfarb Yigal, Zimhony Oren. Infective endocarditis and thromboses due to antiphospholipid syndrome following acute Q fever. *Lancet 2022;* 399(10330): 1154p.

Yen Hui Ling, Sit Thomas HC, Brackman Christopher J, Chuk Shirley SY, Yung Louise. Transmission of SARS-CoV-2 delta variant (AY.127)

from pet hamsters to humans, leading to onward human-to-human transmission: A case study. *Lancet 2022;* 399(10329): 1070-78p.

Abstract:

Background: Transmission of SARS-CoV-2 from humans to other mammals, including pet animals, has been reported. However, with the exception of farmed mink, there is no previous evidence that these infected animals can infect humans, resulting in sustained human-to-human transmission. Following a confirmed SARS-CoV-2 infection of a pet shop worker, animals in the shop and the warehouse supplying it were tested for evidence of SARS-CoV-2 infection.

Methods: In this case study, viral swabs and blood samples were collected from animals in a pet shop and its corresponding warehouse in Hong Kong. Nasal swab or saliva samples from human COVID-19 patients epidemiologically linked to the pet shop and from subsequent local cases confirmed to be infected by SARS-CoV-2 delta variant were collected. Oral swabs were tested by quantitative RT-PCR (RT-qPCR) for SARS-CoV-2 and blood samples were serologically tested by a surrogate virus neutralisation test and plaque reduction neutralisation test. The SARS-CoV-2 RT-qPCR positive samples were sequenced by next generation viral full genome sequencing using the ISeq sequencing platform (Illumina), and the viral genomes were phylogenetically analysed.

Findings: Eight (50%) of 16 individually tested Syrian hamsters in the pet shop and seven (58%) of 12 Syrian hamsters in the corresponding warehouse were positive for SARS-CoV-2 infection in RT-qPCR or serological tests. None of the dwarf hamsters (n=75), rabbits (n=246), guinea pigs (n=66), chinchillas (n=116), and mice (n=2) were confirmed positive for SARS-CoV-2 in RT-qPCR tests. SARS-CoV-2 viral genomes deduced from human and hamster cases in this incident all belong to the delta variant of concern (AY.127) that had not been circulating locally before this outbreak. The viral genomes obtained from hamsters were phylogenetically related with some sequence heterogeneity. Phylogenetic dating suggests infection in these hamsters occurred around Oct 14, 2021 (95% CI Sept 15 to Nov 9, 2021). Multiple zoonotic transmission events to humans were detected, leading to onward human-to-human transmission.

Interpretation: Pet hamsters can be naturally infected with SARS-CoV-2. The virus can circulate among hamsters and lead to human infections. Both genetic and epidemiological results strongly suggest that there was more than one hamster-to-human transmission event in this study. This incident

also led to onward human transmission. Importation of SARS-CoV-2-infected hamsters was a likely source of this outbreak.

Funding: US National Institutes of Health, Research Grants Council of Hong Kong, Food and Health Bureau, and InnoHK.