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# **PREFACE**

## **Introduction**

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

## **Scope**

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

## **Arrangement of Entries**

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

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

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**(Dr. O.P. Verma)**  
**Librarian**

## **AYUSH & Other System**

**Chattopadhyay Rajat, Gupta Sharmistha, Chakraborty Suman, Saha Sangita, Bhar Kaushik. Preparation and Standardisation of Mother Tincture from *Strychnos potatorum*: A New Drug Source in Homoeopathy. *Homoeopathic Links* 2022; 35(1): 3-9p.**

### **Abstract:**

*Strychnos potatorum* L.f. is a deciduous tree of 12 metre height, belongs to Loganiaceae family under genus *Strychnos* and is commonly distributed throughout India. Its flowering time is from February to May and fruiting time from October to March. This plant contains diaboline as active compound and besides it, terpenoid, cardiac glycoside and phenolic compounds as other phytochemical constituents. Recent study has revealed that the plant's seed has antidiabetic, nephroprotective, hepatoprotective, antipyretic, antineoplastic, antimicrobial and contraceptive properties. Hence different systems of medicine like Ayurveda, Unani and Siddha have included this plant in their pharmacopoeial preparation and use it according to their own principles. Ayurvedic system uses the seed against skin disease, gonorrhoea, fever and inflammation of the eyes. Unani system uses it for treatment of urinary complaints whereas Siddha system uses it for treatment of chronic obstructive pulmonary disease. Genus *Strychnos* is a well-known genus to homoeopathy system. Drugs like *Ignatia* and *Nuxvomica* belong to this genus, but no data till today regarding the above-stated plant are available in the homoeopathic pharmacopoeia of India. So, the objective of this physiochemical study is to search the scope of inclusion of this plant as new medicinal source in homoeopathic system of medicine for the purpose of drug proving. Keeping this objective in our mind, chemical analysis of the ethanolic extract of the seed was done by thin layer chromatography and ultraviolet-visible spectrophotometry, which was followed by preparation and standardisation of mother tincture.

**Christina Niedermann, Thomas Ostermann. On Gardening, Ice Cream, Mental Health, and Movement. *Journal of Integrative and Complementary Medicine* 2022; 28(5): 373-74p.**

**Czakert Judith, Stritter Wiebke, Blakeslee Sarah B, Seifert Georg. Plant Fragrances Are Like Music for Our Senses: A Scoping Review of Aromatherapy in Gynecologic Cancers and Breast Cancer Care. *Journal of Integrative and Complementary Medicine* 2022; 28(5): 377-90p.**

### **Abstract:**

**Introduction:** Essential oil (EO) applications via inhalation and/or absorption through the skin—often referred to as aromatherapy—have particular relevance as complementary to cancer treatment and follow-up care. Aromatherapy is of particular interest for controlling symptoms and

enhancing the general well-being of people with cancer. This is indicated by the increasing number of empirical studies on this topic. Although numerous reviews have summarized the extensive primary research about aromatherapy and cancer, no review on aromatherapy use targeting women with gynecologic and breast cancers currently exists. Our scoping review aims at giving an overview of the state of research about aromatherapy in this specific target group. By summarizing and describing study characteristics, based on methodological decisions and content, we intend to offer implications for future research, focused on the use of EO in women with gynecologic and breast cancers.

**Methods:** A systematic scoping review was conducted, based on the literature, and using the extension of the PRISMA statement for scoping reviews (PRISMA-ScR). The databases PubMed and CINAHL were searched in a multi-stage, iterative process taking the most relevant terms under consideration, given our research interest and Boolean operators. The included studies were analyzed and summarized through (1) a table matrix including categories of interest and (2) qualitative content analysis.

**Results:** One hundred seventy studies were examined, and 10 were included in this review. They show high heterogeneity in how the term aromatherapy is defined, in content, research design, EO used, application, and outcomes. However, all 10 studies exclusively targeted women with breast cancer in different states of cancer treatment.

**Conclusions:** Challenges of research within this field point to the heterogeneous use and classification of the term aromatherapy, the differentiation of the principle of action of EO, the lack of transparency in how EO are reported and described (e.g., botanical names, company, dosage, mixing ratios), and the need to include subjective perceptions. Ten implications for future research based on these challenges are given.

**Daruiche Paulo Sergio Jordao, Canoas Walter Swain, Figueira Katya Aparecida Goncalves, Peres Giovani Bravin. Homeopathy for COVID-19 Prevention: Report of an Intervention at a Brazilian Service Sector Company. *Homeopathy*: 2022; 111(2): 105-12p.**

**Abstract:**

**Background:** COVID-19 quickly became a serious public health problem worldwide, with serious economic and social repercussions. Homeopaths around the world have been studying to find a genus epidemicus (GE) medicine that might help in the prevention and treatment of this disease.

**Objective:** To compare the incidence of COVID-19 between employees who received or did not receive a homeopathic GE medicine for disease prevention.

**Methods:** Retrospective cohort analysis. The study population comprised all employees of a service sector company in São Paulo, Brazil, and followed

up by the corporate Occupational Health department. Intervention consisted of administering Arsenicum album 30cH in a one-weekly dose. Primary outcome was incidence of COVID-19 during 3-months' follow-up (April to July, 2020).

**Results:** We analyzed 1,642 of 1,703 employees without previous diagnosis of COVID-19 at onset of the study period: 53.34% of employees were referred to telework at home and did not receive intervention (Group 1, G1); 24.66% remained working on-premises in the state of São Paulo and received the intervention (Group 2, G2); 21.98% remained working on company premises in other states and did not receive intervention (Group 3, G3). Incidence rate of COVID-19 was respectively 13.35%, 0.74%, and 67.87% ( $p < 0.001$ ). The odds ratio of being infected in (1) G3 versus G1 was 13.70 (95% confidence interval [CI], 10.21 to 18.39), (2) G3 versus G2 was 283.02 (95% CI, 88.98 to 900.18), and (3) G1 versus G2 was 20.66 (95% CI, 6.53 to 65.39).

**Limitations:** The present is a retrospective analysis of a real-world experience. We could not ensure direct observed treatment, and neither could we control adherence to general prevention measures outside company premises.

**Conclusion:** The incidence of COVID-19 was significantly lower amongst on-premises employees who received the GE medication in comparison to workers who did not receive the intervention (those either at other company premises or teleworking at home).

**Deepthi Gilla, Sreeja KR, Resmy R. Autism Spectrum Disorder Managed with Individualised Homoeopathic Medicine: Analysis of 20 Cases. *Homoeopathic Links* 2022; 35(1): 70-75p.**

**Abstract:**

**Background:** Autism spectrum disorder (ASD) is an umbrella term used to describe a constellation of early-appearing social communication deficits and repetitive sensorymotor behaviours. There is a dramatic increase in prevalence of ASD in the past few decades. Autism is a potentially lifelong impairing disorder usually managed with complementary therapies, symptomatic behavioural, sensory integration therapies and medical treatments. As there are currently no specific medicines that can address core disabilities of ASD, there is a desperate need to explore new interventions in ASD.

**Objectives:** The aim of this study is to assess the effectiveness of homoeopathic medicines in the usual care setting, i.e. regular OPD, for the management of ASD using Autism Treatment Evaluation Checklist (ATEC).

**Materials and Methods:** The present study is a case series analysis of 20 cases diagnosed as ASD and evaluated with ATEC in the outpatient unit of Department of Psychiatry, National Homoeopathy Research Institute in

Mental Health. Individualised homoeopathic medicines were prescribed based on classical homoeopathic principles. Wilcoxon signed-rank test was used to compare ATEC scores at baseline to end of 12 months.

**Results:** The median baseline ATEC score of 110.0 (116.0–94.5) reduced to 33.5 (61.75–25.0) at  $p < 0.001$ , with an effect size of 0.88. There was statistically significant difference in all domains of speech language communication, sociability, sensory/cognitive awareness and health/physical/behaviour when compared from baseline to end of 12 months. Calcarea carbonica, Calcarea phosphorica, Carcinosinum, Mercurius solubilis, Natrum muriaticum, Silicea, Theridion, Tuberculinum, Zincum metallicum etc. were commonly indicated homoeopathic medicines.

**Conclusion:** Individualised Homoeopathic medicines are effective in the management of ASD. Well planned, methodically rigorous research is warranted to corroborate the evidence.

**Dewan Deepti. Case of Tinea Corporis Treated with Homoeopathy. *Homoeopathic Links* 2022; 35(1): 84-85p.**

**Dixit Ashish Kumar, Mukherjee Sukhes, Javed Danish, Giri Nibha. Exploring the Molecular Mechanism of Homoeopathic Medicines against Cancer: A Pragmatic Approach with Narrative Review of Cell Line Studies. *Homoeopathic Links* 2022; 35(1): 37-47p.**

**Abstract:**

**Background:** Cancer (CA) is the second leading cause of death, accounting for one out of every six deaths worldwide. Chemotherapy and radiation treatments have unwanted effects and due to financial constraints are not available to a large portion of the population. Many CA patients turn to homoeopathy to improve their quality of life and to relieve pain caused by illness/conventional treatments.

**Objective:** The review aims to appraise and summarise the findings of various in vitro CA cell line studies on homoeopathic medicines (HMs) and the detailed molecular mechanism behind the anti-CA effects of HMs.

**Methods:** A systematic search was conducted on the major electronic biomedical database PubMed/MEDLINE for articles on homoeopathy and the CA cell line published between 25 June 2011 and 24 June 2021.

**Result:** The searches identified 18 relevant articles. HMs showed cytotoxicity, increase in reactive oxygen species and decrease in mitochondrial membrane potential against CA cells while preserving normal cells. It interacts with deoxyribonucleic acid and up and down-regulation of pro- and anti-apoptotic signalling proteins (p53, caspase-3 and Bax:B-cell lymphoma 2 [Bcl-2]), which all are involved in apoptosis. Increasing the treatment time of CA cells resulted in a higher percentage of cells in the

G0/G1 phase (cell cycle arrest) and also showed inhibition of cell migration. HMs also had a complex effect on gene expression profiles.

**Conclusion:** This review highlights preliminary laboratory evidence that HMs have therapeutic potential for combating the menace of carcinogenesis. More data are needed to show anti-tumour potential in the current setting and therapeutic value in battling CA.

**Ganguly Subhasish, Mukherjee Shyamal Kumar, Pal Rajat Kumar, Hossain Md. Sakhawat, Saha Sangita, Adhikary Soumendu et al. Varying Genus Epidemicus Remedies in Different Waves of the COVID-19 Pandemic in West Bengal, India. *Homeopathy*: 2022; 111(2): 152-53p.**

**Guo Xiaoli, Zhang Xiaoying, Sun Meng, Yu Lingxiao, Qian Chuan, Zhang Jidan et al. Modulation of Brain Rhythm Oscillations by Xingnao Kaiqiao Acupuncture Correlates with Stroke Recovery: A Randomized Control Trial. *Journal of Integrative and Complementary Medicine* 2022; 28(5): 436-44p.**

**Abstract:**

**Objectives:** In China, Xingnao Kaiqiao (XNKQ) acupuncture has been widely used for stroke treatment. However, its electrophysiological mechanism remains unclear. Hence, this study aims to study how XNKQ acupuncture modulates brain rhythm oscillations of stroke patients, and investigate its correlation with stroke recovery.

**Design:** Randomized control trial.

**Subjects:** Twenty (sub)acute ischemic stroke patients were enrolled and randomly assigned to two groups (an acupuncture group [AG] [n = 10] and a control group [CG] [n = 10]), and four patients (two patients in each group) dropped out of the study.

**Interventions:** All patients received conventional treatments, and the patients in AG received additional XNKQ acupuncture treatment once a day for 10 consecutive days.

**Outcome measures:** Before treatment, 14 days after, and 30 days after treatment onset, their movement impairments and neurologic deficits were measured using the National Institute of Health Stroke Scale (NIHSS), the Fugl-Meyer (FM) Scale, the Modified Rankin Scale (mRS), and the Modified Barthel Index (MBI), and their electroencephalogram data were recorded.

**Results:** Compared with the CG, the AG showed more improvement in FM scores ( $p = 0.02$ ), as well as decreased relative delta power and increased relative alpha power after 2 weeks' treatment. The decrease of the relative delta power and the increase of the relative alpha power in the ipsilesional



frontal area were significantly correlated with the FM improvement (F5, F7, FC1, and Fz electrodes, all  $|r| > 0.517$ ,  $p < 0.040$ ).

**Conclusions:** The curative effect of XNKQ acupuncture related to its electrophysiological modulation.

**Huang Chia Yu, Wu Mei Yao, Huang Ming Cheng, Zimmerman Greg, Yang Liang Yo, Lin Cheng Li et al. Association Between Acupuncture Therapies and Reduced Fracture Risk in Patients with Osteoarthritis: A Nationwide Retrospective Matched Cohort Study. *Journal of Integrative and Complementary Medicine* 2022; 28(5): 418-26p.**

**Abstract:**

**Objective:** The aim of this study is to investigate the association between acupuncture therapy and the risk of fracture in patient with osteoarthritis (OA).

**Design:** The authors performed a 1:1 propensity score-matched cohort study to analyze patient with OA between January 1, 1997 and December 31, 2010 through the Taiwanese National Health Insurance Research Database. Patients who received acupuncture therapy from the initial date of diagnosis of OA to December 31, 2010 were included in the acupuncture cohort. Patients who did not receive acupuncture during the same follow-up period were defined as the no-acupuncture cohort. A Cox regression model was used to adjust for sex, age, comorbidities, prescription, and surgical experiences. Hazard ratios (HRs) were compared between the two cohorts.

**Results:** A total of 3416 patients were identified after 1:1 propensity score matching. The patients had similar basic characteristics. In the final analysis, 292 patients in the acupuncture cohort (30.06 per 1000 person-years) and 431 patients in the no-acupuncture cohort (56.08 per 1000 person-years) developed fractures (adjusted HRs 0.57, 95% confidence interval 0.49–0.67). A reduced cumulative incidence of fracture was found in the acupuncture cohort (log-rank test,  $p < 0.001$ ). The association between acupuncture and reducing the fracture incidence was independent of sex, comorbidities, drugs use, and surgical experiences.

**Conclusion:** Their results revealed the association between acupuncture therapies and a reduced incidence of fracture development in patients with OA. This finding provides noteworthy ideas for further research.

**Jeitler Michael, Michalsen Andreas, Schwartz Andreas, Kessler Christian S, Koppold Liebscher Daniela, Julia Grasmé et al. Effects of a Supplement Containing a Cranberry Extract on Recurrent Urinary Tract Infections and Intestinal Microbiota: A Prospective, Uncontrolled Exploratory Study. *Journal of Integrative and Complementary Medicine* 2022; 28(5): 399-406p.**

## **Abstract:**

**Aim:** Cranberries (*Vaccinium macrocarpon*) are traditionally used in prevention of urinary tract infections (UTIs). The authors' aim was to evaluate effects of a supplement containing cranberry extract, pumpkin seed extract, vitamin C, and vitamin B2 on recurrent uncomplicated UTIs in women and their intestinal microbiota.

**Methods:** A prospective, uncontrolled exploratory study was conducted in women with recurrent uncomplicated UTIs. The primary exploratory outcome was the number of UTIs in a 6-month prospective observation period compared with a 6-month retrospective period. Further outcomes included number of antibiotics, quality of life (SF-36), intestinal microbiota (assessed by 16S rRNA amplicon sequencing), and evaluation questions. Parameters were assessed at baseline and after 1, 2, and 7 months (start of intake of cranberry supplement after 1 month for 6 months). p-Values were calculated with the pairwise Wilcoxon signed-rank test for a diversity and permutational multivariate analysis of variance.

**Results:** Twenty-three women (aged  $52.7 \pm 12.4$  years) were included in the study. Participants reported  $2.2 \pm 0.8$  UTIs (at baseline) in the previous 6 months. After 6 months of cranberry intake, participants reported a significant decrease to  $0.5 \pm 0.9$  UTIs ( $p < 0.001$ ). Number of antibiotic therapies was also significantly ( $p < 0.001$ ) reduced by 68% during 6 months of cranberry intake ( $0.14 \pm 0.35$ ) when compared with 6 months retrospectively ( $1.14 \pm 0.71$ ). The SF-36 physical component score increased from  $44.9 \pm 5.5$  at baseline to  $45.7 \pm 4.6$  at 7 months ( $p = 0.16$ ). The SF-36 mental component score decreased slightly from the baseline value of  $46.5 \pm 6.5$  to  $46.2 \pm 6.4$  at 7 months ( $p = 0.74$ ). No significant intragroup mean changes at genus, family, or species level for  $\alpha$  and  $\beta$  diversity within the intestinal microbiota were found. In the evaluation questions, participants rated the cranberry extract positively and considered it beneficial. The supplement intake was safe.

**Conclusions:** This study shows that women with recurrent uncomplicated UTIs benefit from cranberry intake. Future larger clinical studies with further investigation of the mechanisms of action are required to determine the effects of cranberries on participants with uncomplicated UTIs.

**Kaoru Honaga, Yohei Otaka, Kentaro Kaji, Yasuyuki Sakata, Hirokazu Hamano, Hirohiko Nakamura et al. Effects of Citrus depressa Hayata Fruit Extract on Thigh Muscles Mass and Composition in Subacute Stroke Patients: A Double-Blind, Randomized, Controlled Pilot Trial. *Journal of Integrative and Complementary Medicine* 2022; 28(5): 391-98p.**

## **Abstract:**

**Objective:** This pilot study evaluated the effects of Citrus depressa Hayata fruit extract (CFEx) on thigh muscle cross-sectional area (CSA) and

composition in subacute stroke patients with hemiparesis who were undergoing rehabilitation.

**Design and Intervention:** This double-blinded, placebo-controlled, randomized pilot trial included 40 subacute stroke patients with moderate-to-severe hemiparesis, and they were randomly assigned to receive CFEx or placebo supplements for 12 weeks. The thigh muscle CSA was measured by computed tomography as total muscle area defined by Hounsfield units (HU) values of -29 to 150 HU. The total muscle area was divided into muscle area with fat infiltration and normal muscle area to evaluate muscle composition (-29 to 29 and 30 to 150 HU, respectively).

**Results:** At baseline, the total muscle area and normal muscle area in the paretic thigh were lower than those in the nonparetic thigh. The nonparetic normal muscle area was significantly higher in the CFEx group than in the placebo group at 12 weeks, whereas the total muscle area was not different.

**Conclusions:** The thigh muscle CSA and composition in the paretic side have already deteriorated in patients with moderate-to-severe hemiparesis at the subacute stroke stage. CFEx supplementation during rehabilitation might improve the nonparetic thigh muscle composition in subacute stroke patients. Findings of this study are needed to be verified by a large-scale randomized trial since this study was a pilot study with a small sample size. Trial registration: UMIN Clinical Trial Registry (UMIN ID: UMIN000012902).

**Macias Cortes Emma. Menopause is more than Hot Flashes: What is Missing in Homeopathic Research? A Narrative Review. *Homeopathy*: 2022; 111(2): 79-96p.**

**Abstract:**

**Background:** Menopausal complaints are frequently treated with homeopathy in daily practice worldwide. Recently, vasomotor symptoms have been understood to have implications as predictors of other important and long-term outcomes, causing increased risk of mortality and/or disability.

**Methods:** A comprehensive search of the literature was conducted to investigate whether homeopathic treatments for menopausal women with vasomotor symptoms have a positive effect on other important health outcomes associated with menopause, such as cardiovascular disease, neurocognitive impairment, metabolic and mood disorders, or osteoporosis.

**Results:** Though observational studies have shown encouraging results in reducing the severity and frequency of hot flashes in women treated with homeopathy, few randomized controlled trials have shown positive results. In most of the studies using homeopathy, the primary outcome is reduction in the frequency and severity of hot flashes, and other menopausal complaints are assessed secondarily as a part of the symptoms evaluated in the menopausal scales. Quality of life improves with homeopathic

treatments for hot flashes, but there is scarce evidence of the effect of homeopathy on other health outcomes associated with menopause. Limited evidence exists in the case of menopausal women treated with individualized homeopathy for depression and metabolic disorders.

**Conclusion:** A more comprehensive approach for treating menopause in routine homeopathic practice constitutes a valuable opportunity to increase knowledge and high-quality research in this field. Future homeopathic research for menopause should be focused on well-designed, double-blind, placebo-controlled, randomized trials as well as on pragmatic trials to show whether homeopathic treatments for vasomotor symptoms can also improve outcomes that are well-known to increase the risk of mortality and/or disability.

**Madsen Ruy. Great Pain to Break the Shell: A Case of Carbo animalis. *Homeopathic Links* 2022; 35(1): 76-80p.**

**Abstract:**

This is the case of a woman with depression, endometriosis and infertility. The remedy was selected according to the approaches of the contemporary authors of Classical Homeopathy. The result was a physical and mental improvement.

**Mathie Robert T. Refining Research in Homeopathy. *Homeopathy*: 2022; 111(2): 77-78p.**

**Moride Yola. Methodological Considerations in the Assessment of Effectiveness of Homeopathic Care: A Critical Review of the EPI3 Study. *Homeopathy*: 2022; 111(2): 147-51p.**

**Abstract:**

**Background:** EPI3 is an observational study of a representative sample of general practitioners (GPs) and patients in France, demonstrating that patient characteristics differ according to the prescribing preferences of their GPs for homeopathy. For selected conditions (musculoskeletal disorders, sleep disorders, anxiety/depression, upper respiratory tract infections), progression of symptoms and adverse events over follow-up in the homeopathy preference group did not significantly differ from other practice preferences, but there was a two-fold to four-fold lower usage of conventional medicines. The EPI3 study's validity was challenged due to absence of head-to-head comparison of medicines to conclude on a causal association between homeopathy and outcomes.

**Methods:** A critical review of the nine EPI3 publications was conducted, focusing on generalizability, selection bias, outcome measurements and confounding.

**Results:** The conceptual framework of EPI3 rests on a systemic construct, i.e., the homeopathic treatment concept assessed using the type of GP prescribing preference, taking into account the clinical, human and social aspects. The enrollment process enhanced the generalizability of findings. Validated instruments for outcome measurements were used for three conditions, and control of confounding was rigorous.

**Conclusion:** EPI3 was conducted according to best practices. Homeopathy prescribing preference met specific patient needs with less use of conventional medicines and without an apparent loss in therapeutic opportunity.

**Mukherjee Shyamal Kumar, Ganguly Subhasish, Das Satadal, Chatterjee Kalyan Kumar, Naskar Kisor Kumar, Dey Samit et al. Homeopathic Medicines Used as Prophylaxis in Kolkata during the COVID-19 Pandemic: A Community-Based, Cluster-Randomized Trial. *Homeopathy*: 2022; 111(2): 97-104p.**

**Abstract:**

**Introduction:** There is some evidence that homeopathic treatment has been used successfully in previous epidemics, and currently some countries are testing homeoprophylaxis for the coronavirus disease 2019 (COVID-19) pandemic. There is a strong tradition of homeopathic treatment in India: therefore, we decided to compare three different homeopathic medicines against placebo in prevention of COVID-19 infections.

**Methods:** In this double-blind, cluster-randomized, placebo-controlled, four parallel arms, community-based, clinical trial, a 20,000-person sample of the population residing in Ward Number 57 of the Tangra area, Kolkata, was randomized in a 1:1:1:1 ratio of clusters to receive one of three homeopathic medicines (Bryonia alba 30cH, Gelsemium sempervirens 30cH, Phosphorus 30cH) or identical-looking placebo, for 3 (children) or 6 (adults) days. All the participants, who were aged 5 to 75 years, received ascorbic acid (vitamin C) tablets of 500 mg, once per day for 6 days. In addition, instructions on healthy diet and general hygienic measures, including hand washing, social distancing and proper use of mask and gloves, were given to all the participants.

**Results:** No new confirmed COVID-19 cases were diagnosed in the target population during the follow-up timeframe of 1 month—December 20, 2020 to January 19, 2021—thus making the trial inconclusive. The Phosphorus group had the least exposure to COVID-19 compared with the other groups. In comparison with placebo, the occurrence of unconfirmed COVID-19 cases was significantly less in the Phosphorus group (week 1: odds ratio [OR], 0.1; 95% confidence interval [CI], 0.06 to 0.16; week 2: OR, 0.004; 95% CI, 0.0002 to 0.06; week 3: OR, 0.007; 95% CI, 0.0004 to 0.11; week 4: OR, 0.009; 95% CI, 0.0006 to 0.14), but not in the Bryonia or Gelsemium groups.

**Conclusion:** Overall, the trial was inconclusive. The possible effect exerted by Phosphorus necessitates further investigation.

**Nikumbh Sunita, Kukde Abhishek, Patel Manoj, Parekh Bhavik, Nigwekar Anoop, Mittal Renu et al. Outcome of Homoeopathic Intervention in Psychiatric Inpatients Treated in Rural Homoeopathic Hospital, Palghar, Maharashtra, India, 2014–2018: A Retrospective Analysis. *Homoeopathic Links* 2022; 35(1): 18-23p.**

**Abstract:**

**Background:** Rural homoeopathic hospital has been serving the community in and around Palghar for the past 20 years. Through a Central Government Scheme of Centre of Excellence, it received funds for setting up an inpatient psychiatric unit in 2012 whereby it could serve the wider community by admitting the patients with mental illness in a secure ward. This is the second of two papers on the experience of homoeopathic treatment of psychiatric inpatients and details of the outcome of homoeopathic treatment to patients admitted between 2014 and 2018.

**Objective:** Efforts have been made to explore the outcomes of homoeopathic intervention, singly or as adjuvant treatment, for a variety of clinical conditions and to determine the commonly indicated remedies that were found useful.

**Methodology:** A standard operating procedure enabled symptom analysis and evaluation; it also enabled to erect the homoeopathic totality and institute treatment along with conducting the follow-up. Retrospective analysis using Outcome Related to Impact on Daily Living scale helped to establish the results of homoeopathic intervention.

**Results:** An excellent response to homoeopathic intervention was obtained for several clinical conditions like alcohol withdrawal (76.3%), conversion disorder (82.17%), suicide attempt (85.13%), anxiety disorders (84.19%), depressive disorders (75%) and somatoform (85.17%). The rate of improvement in schizophrenia (60%) and epilepsy (22.6%) was lower. The commonly indicated homoeopathic remedies for each clinical condition were identified. This information would help practitioners to acquire knowledge of a pool of remedies from which they could readily determine the similitum.

**Oskan Tasinov, Yoana Kiselova-Kaneva, Desislava Ivanova, Milena Pasheva, Deyana Vankova, Ivanova Diana. Ferrum phosphoricum D12 Treatment Affects J774A.1 Cell Proliferation, Transcription Levels of Iron Metabolism, Antioxidant Defense, and Inflammation-related Genes. *Homeopathy*: 2022; 111(2): 113-20p.**

**Abstract:**

**Background:** Ferrum phosphoricum (FP) is prescribed as a homeopathic remedy to treat the early stages of fever and inflammation in cases of colds or flu, muscle fatigue and anemia. We aimed to analyze the molecular mechanisms of action of FP D12 on cell proliferation and mRNA expression of iron metabolism, antioxidant defense and inflammation-related genes in mouse J774A.1 macrophages.

**Methods:** Cell proliferation was examined using the MTT test. RT-qPCR analyses were performed to estimate gene expression changes. Relative gene expression levels were calculated using the  $2^{-\Delta\Delta C_t}$  method. The effect of treatment using FP D12 tablets was compared with that using placebo tablets (PT).

**Results:** FP D12 in low concentrations (0.0125 mg/mL to 0.025 mg/mL) significantly stimulated proliferation of J774A.1 cells by up to 11% ( $p < 0.01$ ) versus control untreated cells and by up to 40% ( $p < 0.01$ ) versus PT-treated cells in the respective concentration. FP D12 versus PT induced a significant increase in mRNA expression of ferritin light chain (Ftl1) (by 8-fold,  $p < 0.01$ ),  $\beta$ -2-microglobulin (B2m) (by 2.5-fold,  $p < 0.05$ ) and iron-responsive element binding protein 2 (Ireb2) (by 4-fold,  $p < 0.05$ ), and induced a slight decrease in myosin IE (Myo1e) mRNA expression levels (by 0.4-fold,  $p < 0.01$ ) in macrophages. A highly significant ( $r^2 = 0.99$ ,  $p < 0.05$ ) correlation was observed between Ireb2 and B2m transcription levels. Significant stimulation of antioxidant enzyme Gpx-1 (by 1.27-fold,  $p < 0.01$ ) in cells by 0.025 mg/mL FP D12, but a slight decrease (by 0.12-fold,  $p < 0.05$ ) in 0.0125 mg/mL-treated cells, was observed. A significant increase in the gene expression of IL-1 $\beta$  (by 3.5-fold,  $p < 0.05$ ) in macrophages was also detected.

**Conclusion:** Ferrum phosphoricum in D12 dilution potentially exhibits iron retention, antioxidant and immunomodulation activities, possibly by modulating transcription levels of related genes in non-stimulated mouse macrophages.

**Paik Sourindranath, Adhikary Santi. Case of ‘Nasal Papilloma: Cured by Individualised Medicine. *Homoeopathic Links* 2022; 35(1): 82-83p.**

**Prusty Akhyaya Kumar, Bhandari Preeti. Co-morbid Condition of Warts and Vitiligo Treated with Individualized Homeopathy: An Evidence-Based Case Report. *Homeopathy*: 2022; 111(2): 139-46p.**

**Abstract:**

**Background:** Whilst warts and vitiligo are both common skin diseases, their co-morbidity is rare. Here we present a clinical case of warts with vitiligo to illustrate the utility of individualized homeopathic treatment.

**Method:** The homeopathic medicine *Sepia officinalis* was prescribed, based on individualization. During follow-up, changes were documented by photographs. The non-invasive methods ORIDL (Outcome Related to Impact

on Daily Living), VASI (Vitiligo Area and Scoring Index), and VETF (Vitiligo European Task Force) were used to assess treatment progress. Possible causal attribution of outcome with treatment was evaluated using the Modified Naranjo Criteria for Homeopathy (MONARCH).

**Result:** There was a marked improvement of vitiligo, along with the disappearance of warts, as evidenced photographically. VASI and VETF scores were significantly reduced. Main complaints, as well as overall well-being, improved on the ORIDL scale (+3). The MONARCH score (+9) suggested that the clinical improvement was attributable to the homeopathic intervention.

**Conclusion:** The study suggests a significant role for individualized homeopathic treatment in the co-morbidity of warts and vitiligo.

**Raak Christa K, Scharbrodt Wolfram, Berger Bettina, Bussing Arndt, Schonenberg Tu Anna, Martin David D et al. Hypericum perforatum to Improve Postoperative Pain Outcome After Monosegmental Spinal Sequestrectomy (HYPOS): Results of a Randomized, Double-Blind, Placebo-Controlled Trial. *Journal of Integrative and Complementary Medicine* 2022; 28(5): 407-17p.**

**Abstract:**

**Introduction:** Patients undergoing lumbar spine surgery often suffer from severe radicular postoperative pain leading to the prescription of high-dose opioids. In Integrative Medicine, Hypericum perforatum is known as a remedy to relieve pain caused by nerve damage.

**Objectives:** This trial investigated whether homeopathic Hypericum leads to a reduction in postoperative pain and a decrease in pain medication compared with placebo.

**Design:** Randomized double blind, monocentric, placebo controlled clinical trial.

**Settings/Location:** Department of Neurosurgery, Community Hospital Herdecke.

**Subjects:** Inpatients undergoing lumbar sequestrectomy surgery.

**Interventions:** Homeopathic treatment versus placebo in addition to usual pain management.

**Outcomes Measures:** Primary endpoint was pain relief measured with a visual analog scale. Secondary endpoints were the reduction of inpatient postoperative analgesic medication and change in sensory and affective pain perception.

**Results:** Baseline characteristics were comparable between the groups. Pain perception between baseline and day 3 did not significantly differ



between the study arms. With respect to pain medication, total morphine equivalent doses did not differ significantly. However, a statistical trend and a moderate effect ( $d = 0.432$ ) in the decrease of pain medication consumption in favor of the Hypericum group was observed.

**Conclusion:** This is the first trial of homeopathy that evaluated the efficacy of Hypericum C200 after lumbar monosegmental spinal sequestrectomy. Although no significant differences between the groups could be shown, we found that patients who took potentiated Hypericum in addition to usual pain management showed lower consumption of analgesics. Further investigations, especially with regard to pain medication, should follow to better classify the described analgesic reduction.

**Rajvanshy Tanuj, Sharma Humani. Usefulness of Curcuma longa in the Cases of Functional Dyspepsia: A Parallel Arm-Controlled Study. *Homoeopathic Links* 2022; 35(1): 1-2p.**

**Abstract:**

**Background:** Functional dyspepsia is one of the common gastrointestinal (GI) disorders. This prospective experimental, randomised, single-blind placebo-controlled clinical trial was conducted at SKHMC, Jaipur, for a period of 1 year (March 2018– March 2019) with a 3 -month intervention and follow-up period, aiming to ascertain the usefulness of Curcuma longa in the cases of functional dyspepsia.

**Materials and Methods:** In this study, after screening of 220 patients using ROME III diagnostic criteria, 88 cases of functional dyspepsia fulfilling the eligibility criteria were included and enrolled in the study in a ratio of 1:1. Assuming 10% drop-outs to obtain 80 evaluable cases, that is, 40 cases were randomly allocated to experimental group (Curcuma longa), while another 40 cases were allocated to controlled group (Placebo). Both the arms followed dietary and lifestyle modifications. Usefulness of homoeopathic medicine and placebo in cases with functional dyspepsia on day 35 was compared with baseline. Potency used was 30 CH. Assessment and reassessment were done using gastrointestinal symptom (GIS) score.

**Results:** Eighty cases completed the study, in 40 subjects marked improvement was seen in 12 (30%) cases in Curcuma longa group and 00(0%) cases in placebo group, moderate improvement was seen in 8 (20%) cases in Curcuma longa and 01 (2.5%) in placebo group, mild improvement was seen in 6 (15%) cases in Curcuma longa and 2 (5%) cases in placebo group, no relief was seen in 14 (35%) cases in Curcuma longa and 37 (92.5%) cases in placebo group. Functional dyspepsia is found in middle-aged persons of 36 to 45 years, with predominance in females. To analyse the change in the GIS scores of symptoms of functional dyspepsia, paired t-test was applied for both treatment group and control group. It was observed from the paired t-test result that there is a one-point increase in the pre-and post-average GIS score (from 28.65 to 29.65) in the control group and it is not statistically significant ( $t_{1/4} = 0.760$  and  $p_{1/4} = .452$ ). Whereas there is

13.3-point decrease (from 29.55 to 16.25) in the treatment group and it is statistically significant ( $t = 9.347$  and  $p = 0.000$ ).<sup>18</sup>

**Conclusion:** It means medicine is effective in lowering down the GIS score, which was statistically significant to conclude that homoeopathic medicine *Curcuma longa* was effective in the cases of functional dyspepsia.

**Sharma Bindu. Paradigm Shift: Need of the Hour. *Homoeopathic Links* 2022; 35(1): 1-2p.**

**Sharma SR, Sharma Bindu. Immunity: A Step-by-Step Overview. *Homoeopathic Links* 2022; 35(1): 48-55p.**

**Abstract:**

The immune system is an intricate network of various types of cells and proteins that defends the body against infectious diseases. Once the body encounters a pathogenic microorganism, the immune system gets activated and creates a defence mechanism to defeat it and at the same time retains its memory. In future, if the body encounters the same pathogen, it recognises and destroys the pathogen quickly. The whole pathophysiological mechanism involved in this process of defending the body and keeping a record of every pathogen it has encountered, is briefly elucidated. The paper presents a concise description that captures essential nature of immunobiology such as different types of immunity, components of immune system, role of each component and how complement proteins make a functional bridge between two types of immune system. Classification of immunity depicting physiological functioning of its major components and blood cells linked to immune system originating in bone marrow is depicted in flowcharts.

**Shukla Purnima, Misra Purak, Jain Risabh Kumar, Misra Rajiv Kumar. Homoeopathic Treatment of Fibrocystic Breast Diseases: A Case Series. *Homoeopathic Links* 2022; 35(1): 62-69p.**

**Abstract:**

Fibrocystic changes are the most frequently occurring benign conditions of breast disease. Women of 20 to 50 years of age who frequently encounter various forms of stressors have the highest incidence of fibrocystic breast disease (FBD). In cases, where any palpable mass is detected after clinical examination, mammograms and ultrasonography (USG) are the most common investigative tools for the next level of assessment. Five patients with FBD were treated with homoeopathic medicines in our hospital within a period of 3 years under the project: 'Homoeopathic management of benign neoplastic lesions of breast: an evidence-based study'. The diagnosis was based on clinical examination and USG. We followed standard homoeopathic guidelines for the final selection of medicines. Individualised homoeopathic medicines were used to treat these cases. The clinical assessment was done every month and objective assessment was done after

serial USG reports at every 6-month interval. All the patients had notable improvements during treatment as inferred clinically as well as from the USG reports. Few associated symptoms improved too. Assessment of the causal attribution of the outcomes of the treated cases to the homoeopathic intervention was done using Modified Naranjo Criteria. 'Definite' association was found in four out of five cases and one case showed a 'probable' association. Therefore, we may conclude that homoeopathic treatment can be useful in treating FBD. Good-quality clinical trials are needed before making any firm recommendation.

**Sommers Elizabeth, D'Amico Salvatore, Goldstein Laura, Gardiner Paula. Integrative Approaches to Pediatric Chronic Pain in an Urban Safety-Net Hospital: Cost Savings, Clinical Benefits, and Safety. *Journal of Integrative and Complementary Medicine* 2022; 28(5): 445-53p.**

**Abstract:**

**Purpose:** Chronic pain experienced by children and adolescents represents a significant burden in terms of health, quality of life, and economic costs to U.S. families. In 2015, the Boston Medical Center (BMC) Interdisciplinary Pain Clinic initiated an Integrative Medicine (IM) team model to address chronic pain in children. Team members included a pediatrician, child psychologist, physical therapist, acupuncturist, and massage therapist. Children were referred to the pain clinic from primary care and specialty services within BMC, the largest safety-net hospital in the northeastern United States. For this observational assessment, consent and assent were obtained from parents and pediatric patients. Individualized treatment plans were recommended by the IM team.

**Methods:** Self-reported survey and electronic medical record data were collected about socioeconomic demographics, pain, use of medical and IM services, and quality of life. The authors compared health and quality of life indicators and costs of care for each participant from the year before entering the project with these same indicators for the subsequent year.

**Results:** Eighty-three participants were enrolled. Participants ranged in age from 4 to 22 years (mean 14.7 years). Eighty percent of the group were females. Forty-two percent of the sample were white, 30% were Hispanic/Latinx, and 28% were African American. Primary types of pain were abdominal (52%), headache (23%), musculoskeletal (18%), and other (7%). Quality of life indicators improved ( $p = 0.049$ ) and pain interference decreased (Wilcoxon  $p = 0.040$ ). Major economic drivers of cost were emergency department (ED) visits, inpatient hospitalizations, and consultations with medical specialists. For the 46 participants who completed the project, the following total cost savings were noted: \$27,819 (surgeries), \$17,638 (ED visits), \$25,033 (hospitalizations), and \$42,843 (specialist consults). No adverse events were reported.

**Conclusion:** The authors' experience demonstrated that the use of IM approaches in an interdisciplinary team approach is safe, feasible, and acceptable to families. Considerable cost savings were observed in the area of surgical procedures, hospitalizations, and consultations with specialists.

**Suri Mansi, Walter Neha Sylvia, Katnoria Sapna, Gorke Varun, Manchanda Raj Kumar, Khurana Anil et al. Preparation, Standardization and Anti-plasmodial Efficacy of Novel Malaria Nosodes. *Homeopathy*: 2022; 111(2): 121-33p.**

**Abstract:**

**Background:** Resistance to artemisinin and its partner drugs has threatened the sustainability of continuing the global efforts to curb malaria, which urges the need to look for newer therapies to control the disease without any adverse side effects. In the present study, novel homeopathic nosodes were prepared from *Plasmodium falciparum* and also assessed for their in vitro and in vivo anti-plasmodial activity.

**Methods:** Three nosodes were prepared from *P. falciparum* (chloroquine [CQ]-sensitive [3D7] and CQ-resistant [RKL-9] strains) as per the Homeopathic Pharmacopoeia of India, viz. cell-free parasite nosode, infected RBCs nosode, mixture nosode. In vitro anti-malarial activity was assessed by schizont maturation inhibition assay. The in vitro cytotoxicity was evaluated by MTT assay. Knight and Peter's method was used to determine in vivo suppressive activity. Mice were inoculated with *P. berghei*-infected erythrocytes on day 1 and treatment was initiated on the same day. Biochemical, cytokine and histopathological analyses were carried out using standard methods.

**Results:** In vitro: the nosodes exhibited considerable activity against *P. falciparum* with maximum 71.42% (3D7) and 68.57% (RKL-9) inhibition by mixture nosode followed by cell-free parasite nosode (62.85% 3D7 and 60% RKL-9) and infected RBCs nosode (60.61% 3D7 and 57.14% RKL-9). The nosodes were non-toxic to RAW macrophage cell line with >70% cell viability. In vivo: Considerable suppressive efficacy was observed in mixture nosode-treated mice, with  $0.005 \pm 0.001\%$  parasitemia on day 35. Levels of liver and kidney function biomarkers were within the normal range in the mixture nosode-treated groups. Cytokine analysis revealed increased levels of IL-4 and IL-10, whilst a decline in IL-17 and IFN- $\gamma$  was evident in the mixture nosode-treated mice.

**Conclusion:** The mixture nosode exhibited promising anti-malarial activity against *P. falciparum* and *P. berghei*. Biochemical and histopathological studies also highlighted the safety of the nosode for the rodent host. The study provides valuable insight into a novel medicament that has potential for use in the treatment of malaria.

**Taneja Divya, Michael James, Nayak Chaturbhuji. Research Challenges in Homoeopathy. *Homoeopathic Links* 2022; 35(1): 56-61p.**

**Abstract:**

Through this article, we attempt to identify and understand some of the major challenges in homeopathic research and find solutions to overcome them. We have classified and compiled the challenges broadly under the headings of (1) conceptual challenges—difficulties in research arising due to conceptual differences between homeopathy and conventional medicine, in the understanding of disease and its treatment; (2) methodological challenges—such as weak study designs, use of incorrect outcome measures, lack of knowledge of statistics, poor adherence to homeopathic tenets leading to poor remedy selection etc.; (3) difficulties arising due to logistic challenges—lack of well-trained homeopathic physicians in principles of homeopathy as well as research, lack of proper infrastructure leading to hurdles such as limited access to research literature and other necessary resources; (4) research culture—these pertain to the difficulties in homeopathic research stemming from the reluctance of the homeopathic society to assimilate research into its culture. Some steps have been suggested to overcome these challenges, namely improving research education among homeopathic fraternity, ensuring precise application of principles of homeopathy as well as utilising correct research methodology, promoting interdisciplinary communication and encouraging interaction between academicians, researchers and practitioners and taking steps to improve the quality of documentation.

**Travagin David Ronald Parra, Balbuena Melina Castilho de Souza, Coelho Cideli de Paula. Use of Homeopathic Arnica montana 30cH for Postoperative Analgesia in Female Dogs Undergoing Elective Ovariohysterectomy. *Homeopathy*; 2022; 111(2): 134-38p.**

**Abstract:**

**Background:** Ovariohysterectomy (OH) is one of the most frequent elective surgical procedures in routine veterinary practice. Arnica montana is a well-known medicine in phytotherapy, with proven analgesic, anti-inflammatory, antiseptic, healing, antioxidant and immunomodulatory activity. However, there is still a shortage of studies on the action and effects of the homeopathic formulation of the medicine on animals. The aim of this study was to evaluate analgesia with Arnica montana 30cH during the postoperative period after elective OH.

**Methods:** Thirty healthy female dogs, aged 1 to 3 years, weighing 7 to 14 kg, were selected at the Veterinary Hospital in Campo Mourão, Paraná, Brazil. The dogs underwent the surgical procedure with an anaesthetic protocol and analgesia that had the aim of maintaining the patient's wellbeing. After the procedure, they were randomly divided into three groups of 10. One group received Arnica montana 30cH; another received 5% hydroalcoholic solution; and the third group, 0.9% NaCl saline solution. All animals received four drops of the respective solution sublingually and under blinded conditions, every 10 minutes for 1 hour, after the inhalational

anaesthetic had been withdrawn. The Glasgow Composite Measure Pain Scale was used to analyse the effect of therapy. Analysis of variance (ANOVA) followed by the Tukey test was used to evaluate the test data. Statistical differences were deemed significant when  $p \leq 0.05$ .

**Results:** The Arnica montana 30cH group maintained analgesia on average for  $17.8 \pm 3.6$  hours, whilst the hydroalcoholic solution group did so for  $5.1 \pm 1.2$  hours and the saline solution group for  $4.1 \pm 0.9$  hours ( $p \leq 0.05$ ).

**Conclusion:** These data demonstrate that Arnica montana 30cH presented a more significant analgesic effect than the control groups, thus indicating its potential for postoperative analgesia in dogs undergoing OH.

**Yang Eun Mee, Lu Weidong, Giobbie Hurder Anita, Shin Im Hee, Chen Wendy Y, Block Caroline C et al. Auricular Acupuncture During Chemotherapy Infusion in Breast Cancer Patients: A Feasibility Study. *Journal of Integrative and Complementary Medicine* 2022; 28(5): 427-35p.**

#### **Abstract:**

**Introduction:** Breast cancer patients undergoing chemotherapy experience multiple distressing symptoms. The authors investigated the feasibility and potential benefits of auricular acupuncture during chemotherapy infusion in this population.

**Materials and Methods:** Women with stage I–III breast cancer undergoing chemotherapy were enrolled and followed for three chemotherapy cycles. During the first cycle of chemotherapy that participants received after study enrollment, they were provided with educational materials. During the second and third cycles of chemotherapy after enrollment, they received auricular acupuncture. The primary outcome was feasibility, assessed by recruitment, retention, and completion of assessments. Secondary outcomes included symptom burden (Edmonton Symptom Assessment System-Revised Version) and anxiety (State-Trait Anxiety Inventory-State), assessed at four timepoints for each cycle: day 1, pre-education/acupuncture (T1); day 1, post-education/acupuncture (T2); day 2 (T3); and day 5 (T4). Nausea and vomiting (Multinational Association of Supportive Care in Cancer [MASCC] Antiemesis Tool) were assessed on days 2 and 5. Paired t test was used to compare patient-reported outcomes during cycle 1 (education) versus an average of outcomes during cycles 2 and 3 (acupuncture).

**Results:** Twenty-six patients were enrolled, of which 24 completed all acupuncture sessions and 22 completed all outcome assessments. In cycles 2 and 3 versus cycle 1, participants experienced significant reductions in symptom burden (change from T1 to T4:  $-7.9 \pm 13.6$ ,  $p = 0.02$ ), anxiety (change from T1 to T2:  $-3.3 \pm 6.5$ ,  $p = 0.02$ ), and nausea severity on day 2 ( $-1.3 \pm 2.6$ ,  $p = 0.04$ ).

**Conclusions:** The delivery of auricular acupuncture during chemotherapy infusion was feasible and associated with reduction of symptom burden, anxiety, and nausea in breast cancer patients. Larger-scale clinical studies are needed to confirm these findings.

## **Allied System of Medicine**

**Bollyky Thomas J, Hulland Erin N, Barber Ryan M, Collins James K, Dieleman Joseph L. Pandemic preparedness and COVID-19: An exploratory analysis of infection and fatality rates, and contextual factors associated with preparedness in 177 countries, from Jan 1, 2020, to Sept 30, 2021. *Lancet* 2022; 399(10334): 1489-1512p.**

### **Abstract:**

**Background:** National rates of COVID-19 infection and fatality have varied dramatically since the onset of the pandemic. Understanding the conditions associated with this cross-country variation is essential to guiding investment in more effective preparedness and response for future pandemics.

**Methods:** Daily SARS-CoV-2 infections and COVID-19 deaths for 177 countries and territories and 181 subnational locations were extracted from the Institute for Health Metrics and Evaluation's modelling database. Cumulative infection rate and infection-fatality ratio (IFR) were estimated and standardised for environmental, demographic, biological, and economic factors. For infections, we included factors associated with environmental seasonality (measured as the relative risk of pneumonia), population density, gross domestic product (GDP) per capita, proportion of the population living below 100 m, and a proxy for previous exposure to other betacoronaviruses. For IFR, factors were age distribution of the population, mean body-mass index (BMI), exposure to air pollution, smoking rates, the proxy for previous exposure to other betacoronaviruses, population density, age-standardised prevalence of chronic obstructive pulmonary disease and cancer, and GDP per capita. These were standardised using indirect age standardisation and multivariate linear models. Standardised national cumulative infection rates and IFRs were tested for associations with 12 pandemic preparedness indices, seven health-care capacity indicators, and ten other demographic, social, and political conditions using linear regression. To investigate pathways by which important factors might affect infections with SARS-CoV-2, we also assessed the relationship between interpersonal and governmental trust and corruption and changes in mobility patterns and COVID-19 vaccination rates.

**Findings:** The factors that explained the most variation in cumulative rates of SARS-CoV-2 infection between Jan 1, 2020, and Sept 30, 2021, included the proportion of the population living below 100 m (5.4% [4.0–7.9] of variation), GDP per capita (4.2% [1.8–6.6] of variation), and the proportion of infections attributable to seasonality (2.1% [95% uncertainty interval 1.7–2.7] of variation). Most cross-country variation in cumulative infection rates could not be explained. The factors that explained the most variation in COVID-19 IFR over the same period were the age profile of the country (46.7% [18.4–67.6] of variation), GDP per capita (3.1% [0.3–8.6] of variation),



and national mean BMI (1.1% [0.2–2.6] of variation). 44.4% (29.2–61.7) of cross-national variation in IFR could not be explained. Pandemic-preparedness indices, which aim to measure health security capacity, were not meaningfully associated with standardised infection rates or IFRs. Measures of trust in the government and interpersonal trust, as well as less government corruption, had larger, statistically significant associations with lower standardised infection rates. High levels of government and interpersonal trust, as well as less government corruption, were also associated with higher COVID-19 vaccine coverage among middle-income and high-income countries where vaccine availability was more widespread, and lower corruption was associated with greater reductions in mobility. If these modelled associations were to be causal, an increase in trust of governments such that all countries had societies that attained at least the amount of trust in government or interpersonal trust measured in Denmark, which is in the 75th percentile across these spectrums, might have reduced global infections by 12.9% (5.7–17.8) for government trust and 40.3% (24.3–51.4) for interpersonal trust. Similarly, if all countries had a national BMI equal to or less than that of the 25th percentile, our analysis suggests global standardised IFR would be reduced by 11.1%.

**Interpretation:** Efforts to improve pandemic preparedness and response for the next pandemic might benefit from greater investment in risk communication and community engagement strategies to boost the confidence that individuals have in public health guidance. Our results suggest that increasing health promotion for key modifiable risks is associated with a reduction of fatalities in such a scenario.

**Funding:** Bill & Melinda Gates Foundation, J Stanton, T Gillespie, J and E Nordstrom, and Bloomberg Philanthropies.

**Emery Jon, Butow Phyllis, Lai Kwon Julia, Nekhlyudov Larissa, Jefford Michael. Management of common clinical problems experienced by survivors of cancer. *Lancet* 2022; 399(10334): 1537-50p.**

**Abstract:**

Improvements in early detection and treatment have led to a growing prevalence of survivors of cancer worldwide. Models of care fail to address adequately the breadth of physical, psychosocial, and supportive care needs of those who survive cancer. In this Series paper, we summarise the evidence around the management of common clinical problems experienced by survivors of adult cancers and how to cover these issues in a consultation. Reviewing the patient's history of cancer and treatments highlights potential long-term or late effects to consider, and recommended surveillance for recurrence. Physical consequences of specific treatments to identify include cardiac dysfunction, metabolic syndrome, lymphoedema, peripheral neuropathy, and osteoporosis. Immunotherapies can cause specific immune-related effects most commonly in the gastrointestinal tract, endocrine system, skin, and liver. Pain should be screened for and requires assessment of potential causes and non-pharmacological and

pharmacological approaches to management. Common psychosocial issues, for which there are effective psychological therapies, include fear of recurrence, fatigue, altered sleep and cognition, and effects on sex and intimacy, finances, and employment. Review of lifestyle factors including smoking, obesity, and alcohol is necessary to reduce the risk of recurrence and second cancers. Exercise can improve quality of life and might improve cancer survival; it can also contribute to the management of fatigue, pain, metabolic syndrome, osteoporosis, and cognitive impairment. Using a supportive care screening tool, such as the Distress Thermometer, can identify specific areas of concern and help priorities areas to cover in a consultation.

**Farzadfar Farshad, Naghavi Mohsen, Sepanlou Sadaf G, Moghaddam Sahar Saeedi, Larijani Bagher. Health system performance in Iran: A systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2022; 399(10335): 1625-45p.**

**Abstract:**

**Background:** Better evaluation of existing health programmes, appropriate policy making against emerging health threats, and reducing inequalities in Iran rely on a comprehensive national and subnational breakdown of the burden of diseases, injuries, and risk factors.

**Methods:** In this systematic analysis, we present the national and subnational estimates of the burden of disease in Iran using the Global Burden of Disease Study 2019. We report trends in demographics, all-cause and cause-specific mortality, as well as years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life-years (DALYs) caused by major diseases and risk factors. A multi-intervention segmented-regression model was used to explore the overall impact of health sector changes and sanctions. For this analysis, we used a variety of sources and reports, including vital registration, census, and survey data to provide estimates of mortality and morbidity at the national and subnational level in Iran.

**Findings:** Iran, which had 84·3 million inhabitants in 2019, had a life expectancy of 79·6 years (95% uncertainty interval 79·2–79·9) in female individuals and 76·1 (75·6–76·5) in male individuals, an increase compared with 1990. The number of DALYs remained stable and reached 19·8 million (17·3–22·6) in 2019, of which 78·1% were caused by non-communicable diseases (NCDs) compared with 43·0% in 1990. During the study period, age-standardised DALY rates and YLL rates decreased considerably; however, YLDs remained nearly constant. The share of age-standardised YLDs contributing to the DALY rate steadily increased to 44·5% by 2019. With regard to the DALY rates of different provinces, inequalities were decreasing. From 1990 to 2019, although the number of DALYs attributed to all risk factors decreased by 16·8%, deaths attributable to all risk factors substantially grew by 43·8%. The regression results revealed a significant negative association between sanctions and health status.

**Interpretation:** The Iranian health-care system is encountering NCDs as its new challenge, which necessitates a coordinated multisectoral approach. Although the Iranian health-care system has been successful to some extent in controlling mortality, it has overlooked the burden of morbidity and need for rehabilitation. We did not capture alleviation of the burden of diseases in Iran following the 2004 and 2014 health sector reforms; however, the sanctions were associated with deaths of Iranians caused by NCDs.

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

**Jefford Michael, Howell Doris, Li Qiuping, Lisy Karolina, Emery Jon. Improved models of care for cancer survivors. *Lancet* 2022; 399(10334): 1551-60p.**

**Abstract:**

The number of survivors of cancer is increasing substantially. Current models of care are unsustainable and fail to address the many unmet needs of survivors of cancer. Numerous trials have investigated alternate models of care, including models led by primary-care providers, care shared between oncology specialists and primary-care providers, and care led by oncology nurses. These alternate models appear to be at least as effective as specialist-led care and are applicable to many survivors of cancer. Choosing the most appropriate care model for each patient depends on patient-level factors (such as risk of longer-term effects, late effects, individual desire, and capacity to self-manage), local services, and health-care policy. Wider implementation of alternative models requires appropriate support for non-oncologist care providers and endorsement of these models by cancer teams with their patients. The COVID-19 pandemic has driven some changes in practice that are more patient-centered and should continue. Improved models should shift from a predominant focus on detection of cancer recurrence and seek to improve the quality of life, functional outcomes, experience, and survival of survivors of cancer, reduce the risk of recurrence and new cancers, improve the management of comorbidities, and reduce costs to patients and payers. This Series paper focuses primarily on high-income countries, where most data have been derived. However, future research should consider the applicability of these models in a wider range of health-care settings and for a wider range of cancers.

**Makoni Munyaradzi. Hope for access to abortion in Kenya. *Lancet* 2022; 399(10334): 1456p.**

**Malaria in 2022: A year of opportunity. *Lancet* 2022; 399(10335): 1573p.**

**Menni Cristina, Valdes Ana M, Polidori Lorenzo, Antonelli Michela, Spector Tim D. Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of**

**omicron and delta variant dominance: A prospective observational study from the ZOE COVID Study. *Lancet* 2022; 399(10335): 1618-24p.**

**Abstract:**

**Background:** The SARS-CoV-2 variant of concern, omicron, appears to be less severe than delta. We aim to quantify the differences in symptom prevalence, risk of hospital admission, and symptom duration among the vaccinated population.

**Methods:** In this prospective longitudinal observational study, we collected data from participants who were self-reporting test results and symptoms in the ZOE COVID app (previously known as the COVID Symptoms Study App). Eligible participants were aged 16–99 years, based in the UK, with a body-mass index between 15 and 55 kg/m<sup>2</sup>, had received at least two doses of any SARS-CoV-2 vaccine, were symptomatic, and logged a positive symptomatic PCR or lateral flow result for SARS-CoV-2 during the study period. The primary outcome was the likelihood of developing a given symptom (of the 32 monitored in the app) or hospital admission within 7 days before or after the positive test in participants infected during omicron prevalence compared with those infected during delta prevalence.

**Findings:** Between June 1, 2021, and Jan 17, 2022, we identified 63 002 participants who tested positive for SARS-CoV-2 and reported symptoms in the ZOE app. These patients were matched 1:1 for age, sex, and vaccination dose, across two periods (June 1 to Nov 27, 2021, delta prevalent at >70%; n=4990, and Dec 20, 2021, to Jan 17, 2022, omicron prevalent at >70%; n=4990). Loss of smell was less common in participants infected during omicron prevalence than during delta prevalence (16·7% vs 52·7%, odds ratio [OR] 0·17; 95% CI 0·16–0·19, p<0·001). Sore throat was more common during omicron prevalence than during delta prevalence (70·5% vs 60·8%, 1·55; 1·43–1·69, p<0·001). There was a lower rate of hospital admission during omicron prevalence than during delta prevalence (1·9% vs 2·6%, OR 0·75; 95% CI 0·57–0·98, p=0·03).

**Interpretation:** The prevalence of symptoms that characterise an omicron infection differs from those of the delta SARS-CoV-2 variant, apparently with less involvement of the lower respiratory tract and reduced probability of hospital admission. Our data indicate a shorter period of illness and potentially of infectiousness which should impact work–health policies and public health advice.

**Funding:** Wellcome Trust, ZOE, National Institute for Health Research, Chronic Disease Research Foundation, National Institutes of Health, and Medical Research Council.

**Offshoring the asylum process: A dangerous move for health. *Lancet* 2022; 399(10336): 1669p.**

**Saji Hisashi, Okada Morihito, Tsuboi Masahiro, Nakajima Ryu, Asamura Hisao. Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): A multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial. *Lancet* 2022; 399(10335): 1607-17p.**

**Abstract:**

**Background:** Lobectomy is the standard of care for early-stage non-small-cell lung cancer (NSCLC). The survival and clinical benefits of segmentectomy have not been investigated in a randomised trial setting. We aimed to investigate if segmentectomy was non-inferior to lobectomy in patients with small-sized peripheral NSCLC.

**Methods:** We conducted this randomised, controlled, non-inferiority trial at 70 institutions in Japan. Patients with clinical stage IA NSCLC (tumour diameter  $\leq 2$  cm; consolidation-to-tumour ratio  $>0.5$ ) were randomly assigned 1:1 to receive either lobectomy or segmentectomy. Randomisation was done via the minimisation method, with balancing for the institution, histological type, sex, age, and thin-section CT findings. Treatment allocation was not concealed from investigators and patients. The primary endpoint was overall survival for all randomly assigned patients. The secondary endpoints were postoperative respiratory function (6 months and 12 months), relapse-free survival, proportion of local relapse, adverse events, proportion of segmentectomy completion, duration of hospital stay, duration of chest tube placement, duration of surgery, amount of blood loss, and the number of automatic surgical staples used. Overall survival was analysed on an intention-to-treat basis with a non-inferiority margin of 1.54 for the upper limit of the 95% CI of the hazard ratio (HR) and estimated using a stratified Cox regression model. This study is registered with UMIN Clinical Trials Registry, UMIN000002317.

**Findings:** Between Aug, 10, 2009, and Oct 21, 2014, 1106 patients (intention-to-treat population) were enrolled to receive lobectomy (n=554) or segmentectomy (n=552). Patient baseline clinicopathological factors were well balanced between the groups. In the segmentectomy group, 22 patients were switched to lobectomies and one patient received wide wedge resection. At a median follow-up of 7.3 years (range 0.0–10.9), the 5-year overall survival was 94.3% (92.1–96.0) for segmentectomy and 91.1% for lobectomy (95% CI 88.4–93.2); superiority and non-inferiority in overall survival were confirmed using a stratified Cox regression model (HR 0.663; 95% CI 0.474–0.927; one-sided  $p < 0.0001$  for non-inferiority;  $p = 0.0082$  for superiority). Improved overall survival was observed consistently across all predefined subgroups in the segmentectomy group. At 1 year follow-up, the significant difference in the reduction of median forced expiratory volume in 1 sec between the two groups was 3.5% ( $p < 0.0001$ ), which did not reach the predefined threshold for clinical significance of 10%. The 5-year relapse-free survival was 88.0% (95% CI 85.0–90.4) for segmentectomy and 87.9% (84.8–90.3) for lobectomy (HR 0.998; 95% CI 0.753–1.323;  $p = 0.9889$ ). The proportions of patients with local relapse were 10.5% for segmentectomy

and 5.4% for lobectomy ( $p=0.0018$ ). 52 (63%) of 83 patients and 27 (47%) of 58 patients died of other diseases after lobectomy and segmentectomy, respectively. No 30-day or 90-day mortality was observed. One or more postoperative complications of grade 2 or worse occurred at similar frequencies in both groups (142 [26%] patients who received lobectomy, 148 [27%] who received segmentectomy).

**Interpretation:** To our knowledge, this study was the first phase 3 trial to show the benefits of segmentectomy versus lobectomy in overall survival of patients with small-peripheral NSCLC. The findings suggest that segmentectomy should be the standard surgical procedure for this population of patients.

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**Tonorezos Emily S, Cohn Richard J, Glaser Adam W, Lewin Jeremy, Oeffinger Kevin C. Long-term care for people treated for cancer during childhood and adolescence. *Lancet* 2022; 399(10334): 1561-72p.**

**Abstract:**

Worldwide advances in treatment and supportive care for children and adolescents with cancer have resulted in an increasing population of survivors growing into adulthood. Yet, this population is at very high risk of late occurring health problems, including significant morbidity and early mortality. Unique barriers to high-quality care for this group include knowledge gaps among both providers and survivors as well as fragmented health-care delivery during the transition from pediatric to adult care settings. Survivors of childhood and adolescent cancer are at risk for a range of late-occurring side-effects from treatment, including cardiac, endocrine, pulmonary, fertility, renal, psychological, cognitive, and socio-developmental impairments. Care coordination and transition to adult care are substantial challenges, but can be empowering for survivors and improve outcomes, and could be facilitated by clear, effective communication and support for self-management. Resources for adult clinical care teams and primary care providers include late-effects surveillance guidelines and web-based support services.

**Variation in the COVID-19 infection–fatality ratio by age, time, and geography during the pre-vaccine era: A systematic analysis. *Lancet* 2022; 399(10334): 1469-88p.**

**Abstract:**

**Background:** The infection–fatality ratio (IFR) is a metric that quantifies the likelihood of an individual dying once infected with a pathogen. Understanding the determinants of IFR variation for COVID-19, the disease caused by the SARS-CoV-2 virus, has direct implications for mitigation efforts with respect to clinical practice, non-pharmaceutical interventions,

and the prioritisation of risk groups for targeted vaccine delivery. The IFR is also a crucial parameter in COVID-19 dynamic transmission models, providing a way to convert a population's mortality rate into an estimate of infections.

**Methods:** We estimated age-specific and all-age IFR by matching seroprevalence surveys to total COVID-19 mortality rates in a population. The term total COVID-19 mortality refers to an estimate of the total number of deaths directly attributable to COVID-19. After applying exclusion criteria to 5131 seroprevalence surveys, the IFR analyses were informed by 2073 all-age surveys and 718 age-specific surveys (3012 age-specific observations). When seroprevalence was reported by age group, we split total COVID-19 mortality into corresponding age groups using a Bayesian hierarchical model to characterise the non-linear age pattern of reported deaths for a given location. To remove the impact of vaccines on the estimated IFR age pattern, we excluded age-specific observations of seroprevalence and deaths that occurred after vaccines were introduced in a location. We estimated age-specific IFR with a non-linear meta-regression and used the resulting age pattern to standardise all-age IFR observations to the global age distribution. All IFR observations were adjusted for baseline and waning antibody-test sensitivity. We then modelled age-standardised IFR as a function of time, geography, and an ensemble of 100 of the top-performing covariate sets. The covariates included seven clinical predictors (eg, age-standardised obesity prevalence) and two measures of health system performance. Final estimates for 190 countries and territories, as well as subnational locations in 11 countries and territories, were obtained by predicting age-standardised IFR conditional on covariates and reversing the age standardisation.

**Findings:** We report IFR estimates for April 15, 2020, to January 1, 2021, the period before the introduction of vaccines and widespread evolution of variants. We found substantial heterogeneity in the IFR by age, location, and time. Age-specific IFR estimates form a J shape, with the lowest IFR occurring at age 7 years (0.0023%, 95% uncertainty interval [UI] 0.0015–0.0039) and increasing exponentially through ages 30 years (0.0573%, 0.0418–0.0870), 60 years (1.0035%, 0.7002–1.5727), and 90 years (20.3292%, 14.6888–28.9754). The countries with the highest IFR on July 15, 2020, were Portugal (2.085%, 0.946–4.395), Monaco (1.778%, 1.265–2.915), Japan (1.750%, 1.302–2.690), Spain (1.710%, 0.991–2.718), and Greece (1.637%, 1.155–2.678). All-age IFR varied by a factor of more than 30 among 190 countries and territories. After age standardisation, the countries with the highest IFR on July 15, 2020, were Peru (0.911%, 0.636–1.538), Portugal (0.850%, 0.386–1.793), Oman (0.762%, 0.381–1.399), Spain (0.751%, 0.435–1.193), and Mexico (0.717%, 0.426–1.404). Subnational locations with high IFRs also included hotspots in the UK and southern and eastern states of the USA. Sub-Saharan African countries and Asian countries generally had the lowest all-age and age-standardised IFRs. Population age structure accounted for 74% of logit-scale variation in IFRs estimated for 39 in-sample countries on July 15, 2020. A post-hoc analysis showed that high rates of transmission in the care home population might

account for higher IFRs in some locations. Among all countries and territories, we found that the median IFR decreased from 0·466% (interquartile range 0·223–0·840) to 0·314% (0·143–0·551) between April 15, 2020, and Jan 1, 2021.

**Interpretation:** Estimating the IFR for global populations helps to identify relative vulnerabilities to COVID-19. Information about how IFR varies by age, time, and location informs clinical practice and non-pharmaceutical interventions like physical distancing measures, and underpins vaccine risk stratification. IFR and mortality risk form a J shape with respect to age, which previous research, such as that by Glynn and Moss in 2020, has identified to be a common pattern among infectious diseases. Understanding the experience of a population with COVID-19 mortality requires consideration for local factors; IFRs varied by a factor of more than 30 among 190 countries and territories in this analysis. In particular, the presence of elevated age-standardised IFRs in countries with well resourced health-care systems indicates that factors beyond health-care capacity are important. Potential extenuating circumstances include outbreaks among care home residents, variable burdens of severe cases, and the population prevalence of comorbid conditions that increase the severity of COVID-19 disease. During the pre-vaccine period, the estimated 33% decrease in median IFR over 8 months suggests that treatment for COVID-19 has improved over time. Estimating IFR for the pre-vaccine era provides an important baseline for describing the progression of COVID-19 mortality patterns.

**Funding:** Bill & Melinda Gates Foundation, J Stanton, T Gillespie, and J and E Nordstrom.

**Wang Haidong, Paulson Katherine R, Pease Spencer A, Watson Stefanie, Murray Christopher JL. Estimating excess mortality due to the COVID-19 pandemic: A systematic analysis of COVID-19-related mortality, 2020–21. *Lancet* 2022; 399(10334): 1513–36p.**

**Abstract:**

**Background:** Mortality statistics are fundamental to public health decision making. Mortality varies by time and location, and its measurement is affected by well known biases that have been exacerbated during the COVID-19 pandemic. This paper aims to estimate excess mortality from the COVID-19 pandemic in 191 countries and territories, and 252 subnational units for selected countries, from Jan 1, 2020, to Dec 31, 2021.

**Methods:** All-cause mortality reports were collected for 74 countries and territories and 266 subnational locations (including 31 locations in low-income and middle-income countries) that had reported either weekly or monthly deaths from all causes during the pandemic in 2020 and 2021, and for up to 11 year previously. In addition, we obtained excess mortality data for 12 states in India. Excess mortality over time was calculated as observed mortality, after excluding data from periods affected by late



registration and anomalies such as heat waves, minus expected mortality. Six models were used to estimate expected mortality; final estimates of expected mortality were based on an ensemble of these models. Ensemble weights were based on root mean squared errors derived from an out-of-sample predictive validity test. As mortality records are incomplete worldwide, we built a statistical model that predicted the excess mortality rate for locations and periods where all-cause mortality data were not available. We used least absolute shrinkage and selection operator (LASSO) regression as a variable selection mechanism and selected 15 covariates, including both covariates pertaining to the COVID-19 pandemic, such as seroprevalence, and to background population health metrics, such as the Healthcare Access and Quality Index, with direction of effects on excess mortality concordant with a meta-analysis by the US Centers for Disease Control and Prevention. With the selected best model, we ran a prediction process using 100 draws for each covariate and 100 draws of estimated coefficients and residuals, estimated from the regressions run at the draw level using draw-level input data on both excess mortality and covariates. Mean values and 95% uncertainty intervals were then generated at national, regional, and global levels. Out-of-sample predictive validity testing was done on the basis of our final model specification.

**Findings:** Although reported COVID-19 deaths between Jan 1, 2020, and Dec 31, 2021, totalled 5.94 million worldwide, we estimate that 18.2 million (95% uncertainty interval 17.1–19.6) people died worldwide because of the COVID-19 pandemic (as measured by excess mortality) over that period. The global all-age rate of excess mortality due to the COVID-19 pandemic was 120.3 deaths (113.1–129.3) per 100 000 of the population, and excess mortality rate exceeded 300 deaths per 100 000 of the population in 21 countries. The number of excess deaths due to COVID-19 was largest in the regions of south Asia, north Africa and the Middle East, and eastern Europe. At the country level, the highest numbers of cumulative excess deaths due to COVID-19 were estimated in India (4.07 million [3.71–4.36]), the USA (1.13 million [1.08–1.18]), Russia (1.07 million [1.06–1.08]), Mexico (798 000 [741 000–867 000]), Brazil (792 000 [730 000–847 000]), Indonesia (736 000 [594 000–955 000]), and Pakistan (664 000 [498 000–847 000]). Among these countries, the excess mortality rate was highest in Russia (374.6 deaths [369.7–378.4] per 100 000) and Mexico (325.1 [301.6–353.3] per 100 000), and was similar in Brazil (186.9 [172.2–199.8] per 100 000) and the USA (179.3 [170.7–187.5] per 100 000).

**Interpretation:** The full impact of the pandemic has been much greater than what is indicated by reported deaths due to COVID-19 alone. Strengthening death registration systems around the world, long understood to be crucial to global public health strategy, is necessary for improved monitoring of this pandemic and future pandemics. In addition, further research is warranted to help distinguish the proportion of excess mortality that was directly caused by SARS-CoV-2 infection and the changes in causes of death as an indirect consequence of the pandemic.

**Funding:** Bill & Melinda Gates Foundation, J Stanton, T Gillespie, and J and E Nordstrom