

## Scientific evidence and Homeopathy

Homeopathy is more than 200 years old, used by tens of thousands of physicians and over 500 million people worldwide, making it one of the most popular forms of integrated medicine.<sup>1</sup> It is based on the concept of ‘treating like with like’ (in Latin *similia similibus curentur*). Homeopathic treatment aims to stimulate and direct the body’s self-healing capacity by triggering a reaction. The body reacts to stimuli, which have physiological effects (drugs or toxins) by attempting to maintain homeostasis (a stable internal environment). Homeopathy makes therapeutic use of this effect.

Scientific scepticism about homeopathy arises from its use of highly dilute medicines. There is a substantial body of research on this issue: a recent review of basic research on highly dilute homeopathic medicines found 98 replicated experiments, over 70% of replications were positive. Methods used to prepare homeopathic medicines are remarkably similar to some used in cutting-edge nanotechnology and there is growing evidence that nanoparticles play a crucial role in the action of homeopathic medicines.

The research literature includes preclinical and clinical evidence of the effectiveness of homeopathy including historical, observational, comparative effectiveness and randomized clinical trial evidence of good outcomes, greater safety, patient acceptance, accessibility and cost-savings. Homeopathy is often used ‘to treat the patient, not the disease’ strengthening host defences and resilience rather than killing microbes or blocking pathophysiological processes. Here there is overlap with other areas of pharmacology and toxicology including the widely observed phenomenon of hormesis (the paradoxical, stimulatory or beneficial effects of low doses of toxins).<sup>2</sup> A hormetic dose response curve is non-linear: J shaped with a linear dose response relationship at high doses (the shaft) but a reversed dose response, *ie* beneficial or stimulatory (the hook) at low dose. Over 10,000 experiments demonstrating hormesis and important therapeutic implications have been identified.<sup>3</sup>

High quality surveys of use of homeopathy have been conducted in 11 countries.<sup>4</sup> Two surveys in the UK estimated annual use at 3.1% and 9.8%. In France 10.2% of the general population and 18% of children aged 0–4 years use homeopathy annually. 43.5% of French health professionals prescribe homeopathy, often co-prescribing it with conventional medication. Data from the US federal National Health Interview Survey analysed by a team at Harvard show that around 7 million Americans use homeopathy annually, with steady growth. They particularly use it for

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1 Bell IR, Schwartz GE. [Adaptive network nanomedicine: an integrated model for homeopathic medicine](#). *Frontiers in Bioscience (Scholar Ed.)*. 2013;5:685-708

2 Calabrese EJ (2016). Preconditioning is hormesis part I: [Documentation, dose-response features and mechanistic foundations](#). *Pharmacol Res*. 2016 110:242-264.

3 Calabrese V, Giordano J, Signorile A, Laura Ontario M, Castorina S, De Pasquale C, Eckert G, Calabrese EJ (2016). [Major pathogenic mechanisms in vascular dementia: Roles of cellular stress response and hormesis in neuroprotection](#). *J Neurosci Res*. 94(12):1588-1603.

4 Relton, C, Cooper, K, Viksveen, P, Fibert, P, Thomas, K. [Prevalence of homeopathy use by the general population worldwide: a systematic review](#). *Homeopathy*. 2017; 106: 69–78

upper respiratory and ear problems and consider it more effective than nutritional supplements.<sup>5</sup> The demographics of users of homeopathy are consistent internationally: they tend to be female, well educated and to pursue healthy lifestyles.<sup>6</sup>

### **The public health implications of homeopathy**

Polypharmacy (the use of multiple drugs), particularly in the elderly is a major challenge to medicine. This includes opiate analgesics (painkillers), psychotropic drugs (including tranquillisers, antidepressants and sleeping tablets) and antibiotics. The overuse of antibiotics has led to a massive global crisis of antimicrobial resistance: we are running out of effective antibiotics. There is strong research evidence that the integration of homeopathy into medical practice reduces the use of all these hazardous groups of drugs.

The largest comparative effectiveness study of homeopathy published to date is the EPI3 study. A nationwide study in France, coordinated by the Department of Pharmacoepidemiology at the University of Bordeaux, it included 6,379 patients at 804 medical practices. It compared treatment outcomes for patients attending conventional, homeopathic, and mixed practice family physicians in musculoskeletal conditions, upper respiratory tract infection, sleep disorders, anxiety, and depression in terms of clinical benefit, medical care and medication, adverse effects, and loss of therapeutic opportunity. Patients did not differ between groups except for the chronicity of their illness, which was greater in the homeopathic group. *Patients treated by homeopathic physicians showed a similar clinical progression but took about half the amount of non-steroidal anti-inflammatory drugs (NSAIDs) compared to conventionally-treated patients, with fewer NSAID-related adverse events and no loss of therapeutic opportunity.*<sup>7</sup>

Another study in the EPI3 series yielded an analogous result, showing that patients who consult family physicians certified in homeopathy used significantly less antibiotics and antipyretic/anti-inflammatory drugs for upper respiratory tract infections than those who attended family physicians who prescribe only conventional medications, with similar outcomes.<sup>8</sup> *This finding is of considerable public health importance since antimicrobial resistance is now a major global problem.* One of its main causes is overuse of antibiotics for upper respiratory tract infections. Similar results were found in anxiety, depression and sleep disorders.<sup>9</sup>

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5 Dossett, M, Davis, R.B, Kaptchuk, T.J, Yeh, G.Y. [Homeopathy Use by US Adults: Results of a National Survey.](#) American J Public Health. 2016; 106: 743–745

6 Lert F, Grimaldi-Bensouda L, Rouillon F et al. [Characteristics of patients consulting their regular primary care physician according to their prescribing preferences for homeopathy and complementary medicine.](#) Homeopathy (2014);103: 51-57

7 Rossignol M, Begaud B, Engel P, et al. [Impact of physician preferences for homeopathic or conventional medicines on patients with musculoskeletal disorders: results from the EPI3-MSD cohort.](#) Pharmacoepidemiol. Drug Saf. 2012, 21:1093-101.

8 Grimaldi-Bensouda L, Begaud B, Rossignol M, Avouac B, Lert F, et al. (2014) [Management of Upper Respiratory Tract Infections by Different Medical Practices, Including Homeopathy, and Consumption of Antibiotics in Primary Care: The EPI3 Cohort Study in France 2007–2008.](#) PLoS ONE 9(3): e89990

9 Grimaldi-Bensouda L, Abenhaim L, Massol J et al. [Homeopathic medical practice for anxiety and depression in primary care: the EPI cohort study.](#) BMC Complementary and Alternative Medicine (2016) 16:125

## Comparative Effectiveness Research

Comparative effectiveness research examines the effectiveness of treatments in real-world situations, as opposed to the artificial conditions often imposed in randomized controlled trials, comparing outcomes in groups of patients (often known as cohorts) receiving different treatments. There are several such studies of homeopathy, comparing outcomes in various groups of patients attending conventional family physicians, and family physicians who integrate homeopathy in their practice, including those below.

A multinational comparative effectiveness study 30 doctors, at six clinical sites in four countries, including the UK, treating patients with acute respiratory problems. *Response at 14 days was 82.6% for homeopathy compared to 68% for conventional treatment. The rate of adverse events for conventional treatment was 22.3%, versus 7.8% for homeopathy.* A replication of this study included 1,577 patients, of whom 857 received homeopathic and 720 conventional treatment: improvement was significantly faster with homeopathy.<sup>10,11</sup>

Trichard *et al* compared 'homeopathic strategy' against 'antibiotic strategy' in routine medical practice in the management of recurrent acute rhino-pharyngitis in 499 children aged between 18 months and 4 years.<sup>12, 13</sup> *Family physicians using homeopathy had significantly better results in terms of clinical effectiveness, complications, parents' quality of life and time lost from work, for lower cost to social security.*

A group at the Charité University Medical Centre in Berlin compared outcomes between homeopathic and conventional family physicians in chronic diagnoses commonly treated in general practice (adults – headache, low back pain, depression, insomnia, sinusitis; children – atopic asthma, dermatitis, rhinitis).<sup>14,15</sup> 493 patients were treated by 101 homeopathic and 59 conventional family physicians. The patients treated by the two groups of physicians were generally similar. *The conclusion was that patients who sought homeopathic treatment had better outcomes at similar cost.*

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10 Riley D, Fischer M, Singh B, et al. (2001). [Homeopathy and Conventional Medicine: An Outcomes Study Comparing Effectiveness in a Primary Care Setting](#). *Journal of Alternative and Complementary Medicine*, 7:149–159.

11 Haidvogel M, Riley D, Heger M et al. [Homeopathic and conventional treatment for acute respiratory and ear complaints: A comparative study on outcome in the primary care setting](#). *BMC Complement Altern Med*. 2007; 7: 7.

12 Trichard M, Chaufferin G, Nicoloyannis N (2005). [Pharmacoeconomic comparison between homeopathic and antibiotic treatment strategies in recurrent acute rhinopharyngitis in children](#). *Homeopathy*, 94:3–9.

13 Trichard M, Chaufferin G (2004). [Effectiveness, quality of life, and cost of caring for children in France with recurrent acute rhinopharyngitis managed by homeopathic or non-homeopathic General Practitioners](#). *Disease Management and Health Outcomes*, 12:419–427.

14 Witt C, Keil T, Selim D, et al. (2005). [Outcome and costs of homeopathic and conventional treatment strategies: a comparative cohort study in patients with chronic disorders](#). *Complementary Therapies in Medicine*, 13:79-86.

15 Witt CM, Lüdtke R, Baur R, Willich SN (2005). [Homeopathic medical practice: long-term results of a cohort study with 3,981 patients](#). *BMC Public Health*, 5:115.

### **Cost-effectiveness**

Economic analysis of EPI3 data looked at three types of cost: consultation, prescription and total costs. *Overall health expenditure was 20% less for patients consulting homeopathic family physicians in France compared to conventional family physicians.* The lower cost of prescriptions for homeopathic GPs was partially offset by higher consultation costs. Homeopathic physicians prescribed far fewer potentially hazardous drugs including psychotropics, antibiotics and non-steroidal anti-inflammatory drugs.<sup>16</sup>

*In all comparative effectiveness studies of homeopathy, its integration into health care resulted in better outcomes for patients with improved safety. Those that included cost-effectiveness analysis showed no additional cost or reduced costs.*

### **Safety of homeopathy**

Physician and consumer confidence in the safety of homeopathy is justified. *There is no evidence that homeopathic medicines cause serious or long-lasting harm.* A systematic review of the safety of homeopathy, which included a comprehensive search of the English-language literature and enquiries with regulatory authorities, including FDA, concluded: “Homeopathic medicines may provoke adverse effects, but these are generally mild and transient; adverse effects of homeopathy are under-reported; there are cases of 'mistaken identity' where herbal medicines were described as homeopathic. The main risks associated with homeopathy are indirect, relating to the prescriber rather than the medicine.”<sup>17</sup>

### **Basic research: biological models**

There is a substantial body of research in homeopathy using animal models, human cells, plants, and other organisms. The HomBRex database contained details of 2,289 basic research experiments in August 2017. It is maintained by the Carstens Foundation in Stuttgart Germany [www.carstens-stiftung.de/hombrex](http://www.carstens-stiftung.de/hombrex) and is accessible free of charge. Karl Carstens, who endowed it, was President of West Germany 1979 – 1984. Of these experiments 89% reported at least one positive result. Animals were the most often used model system (371), followed by plants (201), human material (92), bacteria and viruses (37), and fungi (32).<sup>18</sup> One of the hallmarks of high quality science is replication. A recent review of biochemical, immunological, botanical, cell biological and zoological experiments on homeopathic dilutions found 98 replicated experiments with over 70% of replications positive.<sup>19</sup>

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16 Colas A, Danno K, Tabar C, Ehreth J, Duru G. [Economic Impact of Homeopathic Practice in General Medicine In France.](#) Health Economics Review (2015) 5:18.

17 Dantas F, Rampes H (2000). [Do homeopathic medicines provoke adverse effects? A systematic review.](#) *Br Homeopath J.* 89:S35–38.

18 Clausen J, van Wijk R, Albrecht H. [Review of the use of high potencies in basic research on homeopathy.](#) *Homeopathy* (2011) 100, 288-292.

19 Endler PC, Bellavite P, Bonamin L, Jäger T, Mazon S. [Replications of fundamental research models in ultra high dilutions 1994 and 2015.](#) *Homeopathy* (2015):104 ;234 - 245

## Basic research: physical and chemical methods

Homeopathic medicines are made from plants, animals (or parts of animals) and other substances serially diluted and vigorously agitated during the manufacturing process. Twelve independent research laboratories in the U.S., France, Italy, Russia, and India have now found that homeopathic medicines studied contain various nanostructures, including source material, silica nanoparticles and gas nanobubbles heterogeneously dispersed in colloidal solution<sup>20, 21, 22, 23</sup>. This work suggests that homeopathic medicines, like modern engineered nanoparticles, act by modulating the allostatic stress response network (allostasis is the process of restoring a stable internal environment), including cytokines, oxidative stress and heat shock proteins<sup>24,25</sup>.

## Clinical trials of homeopathy

By August 2017 1,138 clinical trials of homeopathy had been published. Details can be found on the CORE-HOM database also maintained by the Carstens Foundation and accessible without charge: <http://archiv.carstens-stiftung.de/core-hom>

Four systematic review/meta-analyses of homeopathy for all conditions have been published.<sup>26,27,28</sup> Of these, three reached a positive conclusion: that there is evidence that homeopathy is clinically effective. The exception is the review by Shang *et al.*<sup>46</sup> This meta-analysis was controversial, particularly because its conclusions were based on only eight clinical trials whose identity was concealed until several months after the publication, precluding informed examination of its results. The only undisputed conclusion of this paper is that clinical trials of homeopathy are of higher quality than matched trials of conventional medicine: of 110 clinical trials each of homeopathy and conventional medicine, 21 trials of homeopathy but only 9 trials of conventional medicine were of 'higher quality'.<sup>29 30</sup>

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20 Bhattacharyya SS, Mandal SK, Biswas R, Paul S, Pathak S, Boujedaini N, Belon P, Khuda-Bukhsh AR: [In vitro studies demonstrate anticancer activity of an alkaloid of the plant Gelsemium sempervirens](#). *Exp Biol Med* (Maywood) 2008, 233(12):1591–1601.

21 Chikramane PS, Suresh AK, Bellare JR, Kane SG: [Extreme homeopathic dilutions retain starting materials: A nanoparticulate perspective](#). *Homeopathy* 2010, 99(4):231–242.

22 Upadhyay RP, Nayak C: [Homeopathy emerging as nanomedicine](#). *International Journal of High Dilution Research* 2011, 10(37):299–310.

23 Ives JA, Moffett JR, Arun P, Lam D, Todorov TI, Brothers AB, Anick DJ, Centeno J, Namboodiri MA, Jonas WB: [Enzyme stabilization by glass-derived silicates in glass-exposed aqueous solutions](#). *Homeopathy* 2010, 99(1):15–24

24 Karatsoreos IN, McEwen BS: [Psychobiological allostasis: resistance, resilience and vulnerability](#). *Trends Cogn Sci* 2011, 15(12):576–584.

25 McEwen BS: [Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators](#). *Eur J Pharmacol* 2008, 583(2–3):174–185.

26 Kleijnen J, Knipschild P, ter Riet G (1991). [Clinical trials of homoeopathy](#). *British Medical Journal*, **302**:316–323.

27 Linde K, Clausius N, Ramirez G et al. [Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials](#). *Lancet* 2005; 366:2081–2082.

28 Shang A, Huwiler-Muntener K, Nartey L, et al. (2005). [Are the clinical effects of homeopathy placebo effects? Comparative study of placebo-controlled trials of homeopathy and allopathy](#). *Lancet*, 366:726–732.

29 Fisher P, Berman B, Davidson J, Reilly D, Thompson T et al. [Meta-analysis of homeopathy](#). *Lancet* 2005; 366:2083-4.

30 Lütcke R, Rutten AL. [The conclusions on the effectiveness of homeopathy highly depend on the set of analyzed trials](#). *J Clin Epidemiol* 2008; 61:1197–1204.

A leading Swedish medical researcher remarked: *“To conclude that homeopathy lacks clinical effect, more than 90% of the available clinical trials had to be disregarded. Alternatively, flawed statistical methods had to be applied.”*<sup>31</sup> Higher quality equates to less risk of bias, Mathie *et al* analyzed randomized clinical trials of individualized homeopathy, showing that the highest quality trials yielded positive results.<sup>32</sup>

Systematic reviews of randomized controlled trials of homeopathy in specific clinical situations have also yielded positive results, including: allergies and upper respiratory tract infections (2 systematic reviews),<sup>33,34</sup> Arnica in knee surgery,<sup>35</sup> Childhood diarrhea,<sup>36</sup> Post-operative ileus,<sup>37</sup> Rheumatic diseases,<sup>38</sup> Seasonal allergic rhinitis (hay fever) (2 systematic reviews),<sup>39</sup> 40 and vertigo.<sup>41</sup>

## Conclusion

Sceptics frequently claim that there is no scientific evidence for homeopathy. As this short paper has shown, this is untrue. Although, according to current scientific understanding, it is implausible that the very high dilutions used in homeopathy have effects which are not placebo, there is abundant evidence that they do. Homeopathy is geographically widespread and increasing in popularity. Clinical research and syntheses of such research show it to be safe and effective for a range of conditions. Integrating homeopathy in health care systems is associated with benefits including improved outcomes, less use of drugs including antibiotics, and economic benefits.

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<sup>31</sup> Hahn RG. [Homeopathy: Meta-Analyses of Pooled Clinical Data](#). *Forsch Komplementmed* 2013;20:376–381.

<sup>32</sup> Mathie RT, Lloyd SM, Legg LA, et al. [Randomised placebo-controlled trials of individualised homeopathic treatment: systematic review and meta-analysis](#). *Syst Rev* 2014;3:142.

<sup>33</sup> Bergemann SM, Bornhöft, Bloch D, Vogt-Frank C, Righetti M, Thurneysen A, [Clinical Studies on the Effectiveness of Homeopathy for URTI/A \(Upper Respiratory Tract Infections and Allergic Reactions\)](#). In Bornhöft G, Matthiessen PF (eds), *Homeopathy in Healthcare – Effectiveness, Appropriateness, Safety, Costs*. Springer, Berlin 2011.

<sup>34</sup> Bellavite P, Ortolani R, Pontarollo F, et al. [Immunology and homeopathy. 4. Clinical studies – Part 1](#). *Evidence-based Complementary and Alternative Medicine: eCAM*, 2006; 3: 293–301.

<sup>35</sup> Brinkhaus B, Wilkens JM, Lütke R, et al. [Homeopathic arnica therapy in patients receiving knee surgery: Results of three randomized double-blind trials](#). *Complementary Therapies in Medicine*, 2006; 14: 237–246.

<sup>36</sup> Jacobs J, Jonas WB, Jimenez-Perez M, Crothers D. [Homeopathy for childhood diarrhea: combined results and metaanalysis from three randomized, controlled clinical trials](#). *Pediatric Infectious Disease Journal*, 2003; 22: 229–234.

<sup>37</sup> Barnes J, Resch K-L, Ernst E. [Homeopathy for postoperative ileus? A meta-analysis](#). *Journal of Clinical Gastroenterology*, 1997; 25: 628–633.

<sup>38</sup> Jonas WB, Linde K, Ramirez G. [Homeopathy and rheumatic disease](#). *Rheumatic Disease Clinics of North America*, 2000; 26: 117–123.

<sup>39</sup> Taylor MA, Reilly D, Llewellyn-Jones RH, et al. [Randomized controlled trials of homeopathy versus placebo in perennial allergic rhinitis with overview of four trial series](#). *British Medical Journal*, 2000; 321: 471–476.

<sup>40</sup> Bellavite P, Ortolani R, Pontarollo F, et al. [Immunology and homeopathy. 4. Clinical studies – Part 2](#). *Evidence-based Complementary and Alternative Medicine: eCAM*, 2006; 3: 397–409.

<sup>41</sup> Schneider B, Klein P, Weiser M. [Treatment of vertigo with a homeopathic complex remedy compared with usual treatments: a meta-analysis of clinical trials](#). *Arzneimittelforschung*, 2005; 55: 23–29.

**About the Author**

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