

Homeopathy is a 200-year-old system of medicine, used by nearly 250 thousand physicians and over 500 million people worldwide<sup>1</sup>- making it one of the most popular forms of integrative medicine. It is based on the concept of "treating like with like" (in Latin similia similibus curentur), homeopathy stimulates and directs the body's self-healing mechanisms, or homeostasis.

Scientific skepticism toward homeopathy often arises from its use of highly dilute medicines, and there is a substantial body of research on this issue: a review of basic science research on highly dilute homeopathic medicines found 98 replicated experiments, with over 70% positive. Methods used to prepare homeopathic medicines are remarkably like cutting-edge nanotechnology and there is growing evidence that nanoparticles play a crucial role in the action of homeopathy.

# <sup>1</sup> Bell IR Schwartz GE. <u>Adaptive network nanomedicine: an integrated model for homeopathic medicine</u>. Frontiers in Bioscience (Scholar Ed.) 2013;5(2):685-708.

# Why does homeopathy matter to America?

Data from the federal National Health Interview Survey analyzed by a team at Harvard University show that around 7 million Americans use homeopathy, with steady growth. Users tend to be female, highly educated and pursue healthy lifestyles. They use it primarily for upper respiratory and ear problems and consider it more effective than nutritional supplements.<sup>2</sup> The demographics of users in France and Germany are similar although use is more widespread in those countries.<sup>3</sup>

Polypharmacy (the use of multiple drugs), particularly in the elderly is a major challenge to modern physicians. Opiate analgesics (painkillers), psychotropic drugs (including tranquilizers, antidepressants, and sleeping

<sup>&</sup>lt;sup>2</sup> Dossett, M., Davis, R.B., Kaptchuk, T.J., and Yeh, G.Y. Homeopathy use by US adults: results of a national survey. American J Public Health. 2016; 106: 743-745DOI: <a href="http://dx.doi.org/10.2105/AJPH.2015.303025">http://dx.doi.org/10.2105/AJPH.2015.303025</a>.

<sup>&</sup>lt;sup>3</sup> 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 https://ncbi.nlm.nih.gov/pubmed/24439455

tablets) and antibiotics are widely overused. The overuse of antibiotics has caused a massive global crisis of antimicrobial resistance, and there is strong research evidence suggesting that the integration of homeopathy into medical practice would reduce the need for many of these hazardous drugs.

### **Homeopathic Research**

The research literature offers preclinical and clinical evidence in support of the effectiveness of homeopathic medicines in treating individuals with a wide range of common conditions. Homeopathy shows historical, observational, 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 defenses and resilience rather than killing microbes or blocking pathophysiological processes.



## **Comparative Effectiveness Research**

Comparative effectiveness research examines the results of treatments in real-world situations, as opposed to the artificial conditions often imposed in randomized controlled trials. It compares outcomes in groups of patients (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 led by American physician Dr. David Riley involved 30 doctors, at six clinical sites in four countries, 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>4,5</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>6,7</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.

Witt et al. compared homeopathic and conventional family physicians' outcomes in chronic diagnoses commonly treated in general practice (adults — headache, low back pain, depression, insomnia, sinusitis; children — atopic asthma, dermatitis, rhinitis). 8,9 493 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.

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 from 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. The authors concluded that patients treated by homeopathic physicians showed a similar clinical progression but took about half the

<sup>&</sup>lt;sup>4</sup> 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.

<sup>&</sup>lt;sup>5</sup> Haidvogl 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 doi:

<sup>&</sup>lt;sup>6</sup> 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.

<sup>&</sup>lt;sup>7</sup> Trichard M, Chauffeuring 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.

<sup>&</sup>lt;sup>8</sup> 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*, 13:19-86.

<sup>&</sup>lt;sup>9</sup> Witt CM, Ludtke 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.

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>10</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. **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.<sup>11</sup>

#### **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** (\$78.70 US vs. \$98.91 US). The lower cost of medical prescriptions for homeopathic family physicians was partially offset by higher consultation costs. Homeopathic physicians prescribed far fewer potentially hazardous drugs including psychotropic, antibiotics and non-steroidal anti-inflammatory drugs. <sup>12</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; there are cases of 'mistaken

identity' where herbal medicines were [erroneously] described as homeopathic. The main risks associated with homeopathy are indirect, relating to the prescriber rather than the medicine."<sup>13</sup>

### Basic research: biological models

There is a substantial body of research in homeopathy using animal models, human cells, plants, and other organisms. Of these studies, 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). 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% positive.

# 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, silica, and gas nanobubbles heterogeneously dispersed in colloidal solution. <sup>16,17,18,19</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>20,21</sup>

<sup>&</sup>lt;sup>10</sup> 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.

<sup>&</sup>lt;sup>11</sup> 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. doi:10.1371/journal.Pone.0089990.

<sup>&</sup>lt;sup>12</sup> 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. DOI 10.1186/s13561-015-0055-5.

<sup>&</sup>lt;sup>13</sup> Dantas F, Rampes H (2000). Do homeopathic medicines provoke adverse effects? A systematic review. *Br Homeopath J.* 89:S35-38.

<sup>&</sup>lt;sup>14</sup> Clausen J, van Wijk R, it, Albrecht H. Review of the use of high potencies in basic research on homeopathy. Homeopathy (2011)100, 288-292.

 $<sup>^{\</sup>rm 15}$  Endler PC, Bellavite P, E Bonamin L, Jager T, Mazon S. Replications of fundamental research models in ultra-high dilutions 1994 and 2015. Homeopathy (2015):104; 234-245.

<sup>&</sup>lt;sup>16</sup> 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.

<sup>&</sup>lt;sup>17</sup> Chikramane PS, Suresh AK, Bellare JR, Kane SG: Extreme homeopathic dilutions retain starting materials: A nanoparticulate perspective. Homeopathy 2010, 99(4):231-242.

<sup>&</sup>lt;sup>18</sup> Upadhyay RP, Nayak C: Homeopathy emerging as nanomedicine. International Journal of High Dilution Research 2011, 10(37):299-310.

<sup>&</sup>lt;sup>19</sup> 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.

<sup>&</sup>lt;sup>20</sup> Karatsoreos IN, McEwen BS: Psychobiological allostasis: resistance, resilience and vulnerability. Trends Cogn Sci 2011, 15(12):576-584.

<sup>&</sup>lt;sup>21</sup> 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.

### Clinical trials of homeopathy

There are at least 1,137 clinical trials of homeopathy.<sup>22</sup> Additionally, four systematic reviews/meta-analyses of homeopathy for all conditions have been published.<sup>23, 24, 25</sup> Of these, three reached a positive conclusion: that there is good evidence that homeopathy is clinically effective.

The exception is the review by Shang et al.<sup>26</sup> This meta-analysis was controversial, particularly because its conclusions were based on only eight clinical trials whose identity was not disclosed until several months after the publication of the paper, 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>26, 27</sup>

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>28</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>29</sup>

#### **Conclusion**

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 cost benefits.<sup>30</sup>

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<sup>&</sup>lt;sup>22</sup> http://archiv.carstens-stiftung.de/core-hom/login.php

<sup>&</sup>lt;sup>23</sup> Kleijnen J, Knipschild P, ter Riet G (1991). Clinical trials of homoeopathy *British Medical Journal*, 302:316–323.

<sup>&</sup>lt;sup>24</sup> Linde K, Clausius N, Ramirez G et al. Are the clinical effects of homeopathy placebo effects? *Lancet* 2005; 366:2081–2082.

<sup>&</sup>lt;sup>25</sup> 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.

<sup>&</sup>lt;sup>26</sup> Fisher P, Berman B, Davidson J, Reilly D, Thompson T et al. Meta-analysis of homeopathy. *Lancet* 2005; 366;2083-4.

<sup>&</sup>lt;sup>27</sup> Ludtke 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.

<sup>&</sup>lt;sup>28</sup> Hahn RG. Homeopathy: Meta-Analyses of Pooled Clinical Data. Forsch Komplementmed 2013;20:376-381.

<sup>&</sup>lt;sup>29</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

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