The research evidence base for homeopathy: a fresh assessment of the literature

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**Background.** The claims made for the clinical effects of homeopathy are controversial. The results of several meta-analyses of clinical trials are positive, but they fail in general to highlight specific medical conditions that respond well to homeopathy.

**Aims.** This review examines the cumulative research from randomised and/or double-blind clinical trials (RCTs) in homeopathy for individual medical conditions reported since 1975, and asks the question: What is the weight of the original evidence from published RCTs that homeopathy has an effect that is statistically significantly different from that in a comparative group?

**Method.** Analysis of the 93 substantive RCTs that compare homeopathy either with placebo or another treatment.

**Results.** 50 papers report a significant benefit of homeopathy in at least one clinical outcome measure, 41 that fail to discern any inter-group differences, and two that describe an inferior response with homeopathy. Considering the relative number of research articles on the 35 different medical conditions in which such research has been carried out, the weight of evidence currently favours a positive treatment effect in eight: childhood diarrhoea, fibrositis, hayfever, influenza, pain (miscellaneous), side-effects of radio- or chemotherapy, sprains and upper respiratory tract infection. Based on published research to date, it seems unlikely that homeopathy is efficacious for headache, stroke or warts. Insufficient research prevents conclusions from being drawn about any other medical conditions.

**Conclusions.** The available research evidence emphasises the need for much more and better-directed research in homeopathy. A fresh agenda of enquiry should consider beyond (but include) the placebo-controlled trial. Each study should adopt research methods and outcome measurements linked to a question addressing the clinical significance of homeopathy’s effects. *Homeopathy* (2003) 92, 84–91

**Keywords:** homeopathy; research design; evidence-based medicine; clinical trials

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**Introduction**

To sceptics, homeopathy is an archaic and ineffective method of treatment that proclaims an implausible mode of action. In contrast, the individual and collective experience of homeopathic practitioners paints a convincing picture of its clinical effectiveness. Homeopathy’s possible mechanisms of action remain intangible theories, and it will be important ultimately to substantiate these. The principal issues for the present and immediate future, however, are whether there is compelling research evidence that homeopathy actually does exert a remedial effect, and whether such an effect is remedy-specific.

What comprises ‘compelling evidence’? Many homeopaths are cheerfully sustained by their own successful clinical experience: ‘We know it works, so why do research to prove it?’ However, if homeopathy truly enables people attain better health, then it is
vitaly important that it achieves much wider respect within medicine at large. To do this, homeopathy must convince sceptics ‘by rigorous research evidence’ of its clinical effectiveness. It must also face up to the challenge of demonstrating the specific efficacy of at least some of its medicines. These challenges are best met by data obtained from randomised controlled clinical trials (RCTs), where homeopathy is compared to another intervention or with placebo. Some homeopaths throw up their hands in horror at such a proposition, but new research programmes can grow from observational (cohort) studies, for example, which can inform later RCTs.

A key to success of any study design is that clinical outcome measures must properly reflect the whole-person approach to healthcare that typifies homeopathy. Quality of life assessment and other patient-centred measures, for example, may be at least as important as the measurement of biochemical markers or other physical determinants of health status. After all, in an holistic therapy like homeopathy, the individual symptom- (and thus remedy-) picture often does not equate to a named disease, and so it is inappropriate to measure only disease-specific outcomes in such studies.

Another vital concern is that any statistically significant difference/s between treatment groups in trials should not automatically be equated to clinical importance. It is only the latter that truly matters, and this must be properly accommodated in the power calculations (and thus statistical conclusions) connected with clinical trials. The existing homeopathic research literature has not reflected this issue well—emphasis has been placed on statistical significance with incomplete regard to the clinical value of any inter-group differences observed.

What is the current evidence from which new research in homeopathy can develop? Given the limitations of past research in homeopathy, the optimum question that can be asked of the available evidence base is limited to: What is the weight of the original evidence from published RCTs that homeopathy has an effect that is statistically significantly different from that in a comparative group?

Only since 1975 have rigorous research methods been applied to homeopathy. Prior literature comprised only four minor trials or brief communications. The work reported up to 1997 is captured in the comprehensive meta-analysis of placebo-controlled trials of homeopathy published by Linde et al in The Lancet. Nearly half the trials cited in that paper showed a homeopathic treatment effect statistically significantly greater than that of placebo; none of the trials found placebo more effective than homeopathy. The authors concluded that homeopathy’s clinical effects are not attributable solely to placebo, though they could not single out any medical condition for which homeopathy seemed clearly efficacious.

Since 1997, some 50 new clinical trials or meta-analyses in homeopathy have been published. Many of these newer trials have essentially the same Null hypothesis: ‘Homeopathy has an effect which is not statistically significantly different from that of placebo’; in effect, the Null hypothesis that was rejected by Linde’s meta-analysis. In 2002, the NHS Centre for Reviews and Dissemination based at the University of York, UK, published an overview of all the published systematic reviews and meta-analyses in homeopathic research. The authors conclude: ‘There are currently insufficient data ... to recommend homeopathy as a treatment for any specific condition’. This statement is hardly distinguishable from one of Linde’s conclusions 5 years earlier.

There has been a recent increase in the number of research papers that carry the more original Null hypothesis: ‘Homeopathy has an effect which is not statistically significantly different from that of another active treatment’. Such comparative trials of clinical effectiveness are included in the focus of the present review.

The present paper reports the total currently available statistical evidence from the published research literature for and against the specific efficacy or clinical effectiveness of homeopathy, based on the frequency with which the above two Null hypotheses have been rejected or not rejected in clinical trials. This is neither a meta-analysis nor a formal systematic review—the paucity and heterogeneity of published research in homeopathy limits the value of such formalised approaches. The originality of the present approach lies mainly in the following: (a) it considers the number of individual trials in homeopathy that report outcome statistics, and by type of medical condition studied; (b) it reports only full, published, research papers; (c) it includes comparative as well as placebo-controlled trials. The coverage reflects the entire range of medical conditions in which the effects of homeopathy have been the subject of research and, like Linde et al, it only includes trials that are randomised and/or double-blinded. Based on my review, I conclude by recommending some opportunities for future research development in homeopathy.

Literature search methods

This review examines all published clinical trials on human subjects that appeared in the literature from 1975 until December 2002, and which compared homeopathic treatment with placebo or with another medication, where a randomised and/or double-blind study design has been used. The analysis includes only full papers reporting original research, and excludes conference proceedings, brief communications, book chapters and theses. Reports of case series, clinical outcomes (cohort) studies and other non-controlled investigations are also excluded. All forms of homeopathic intervention are included, from

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Results of literature search and analysis

The database scrutinised and reported here comprises a total of 93 original articles in homeopathic research. Of this total, 79 trials were placebo-controlled, while the remaining 14 compared homeopathy with a conventional medical treatment (controlled comparative trials). Table 1 lists all those medical conditions (35 in total), in 11 broad types, for which there exists at least one published clinical research trial in homeopathy that satisfies the inclusion criteria for this analysis.

There is insufficient evidence either to favour or to find no support for homeopathy (Table 1). Within the group of conditions ‘upper respiratory tract infection’, however, a weight of evidence suggests that homeopathy and conventional medicine (aspirin in both papers concerned) are equally effective in treating the common cold.14,15

Balance of evidence: placebo-controlled trials

Examining the relative number of papers published for each of the three categories or classes of evidence, the present weight of evidence favours homeopathic treatment effectiveness in eight conditions:

- childhood diarrhoea;
- fibrositis (fibromyalgia);
- hayfever/allergic rhinitis;
- influenza;
- pain (of various origins);
- side-effects of radio-/chemotherapy;
- sprains;
- upper respiratory tract infection.

A weight of evidence suggesting homeopathy has no effect above placebo is apparent in three medical conditions:

- headache;
- stroke;
- warts.

For the remaining 20 conditions in which studies have been carried out, there is insufficient weight of evidence either to favour or to find no support for homeopathy (Table 1). Some of these trials are examples of the ‘double positive paradox’,13 where a homeopathy group and a placebo group have indistinguishable results but both manifest some clinical improvement.

Balance of evidence: comparative trials

There is insufficient evidence either to favour or to find no support for homeopathy in nine of the 10 medical conditions in which studies have been carried out (Table 1). Within the group of conditions ‘upper respiratory tract infection’, however, a weight of evidence suggests that homeopathy and conventional medicine (aspirin in both papers concerned) are equally effective in treating the common cold.14,15

Discussion

Number of published trials in homeopathy

The total number of original full research papers over a 27 year time-span (n = 93) is very modest, for research in homeopathy is still in an early stage of development. The largest total number of articles for any particular type of condition is 10 (upper respiratory tract infection). For 12 of the 35 included medical conditions, a single published trial is all that exists. The paucity of research literature is a serious drawback for meta-analyses and formal systematic reviews in homeopathy. In the last 5 years, however,
such syntheses of (usually very few) published trials have provided support for homeopathic treatment in hayfever,\textsuperscript{16} post-operative ileus \textsuperscript{17} and rheumatoid arthritis.\textsuperscript{18} Other meta-analyses or systematic reviews have concluded there is insufficient evidence for or against homeopathy in asthma,\textsuperscript{19} influenza,\textsuperscript{20} muscle soreness,\textsuperscript{21} osteoarthritis,\textsuperscript{22} prophylaxis for migraine or headache\textsuperscript{23} and in tissue trauma treated with \textit{Arnica}.\textsuperscript{24}

Publication bias towards the reporting of 'positive' homeopathic treatment effects has been a well-founded concern, and is properly recognised in meta-analyses,\textsuperscript{6,25,26} though no single trial is individually suspected of biased reporting.\textsuperscript{27} There is thus very likely to be overall exaggeration of reported positive treatment effects in the homeopathic research literature cited in the present review.

### Quality of published trials in homeopathy

This review deliberately does not categorise published trials in homeopathy by their intrinsic scientific quality, for information on this issue is already available. Only 29% of placebo-controlled trials in homeopathy published before 1997 were judged to possess 'high' methodological quality.\textsuperscript{6} A statistical re-evaluation...
of Linde’s meta-analysis noted that treatment effects were larger in smaller studies and in those with inadequate blinding of outcome assessment. Exaggeration of treatment effect can also be expected in the 14 comparative trials highlighted in the present review: the sample sizes of these 14 studies (mean, 97 patients; range, 10–184) are broadly equivalent to those for placebo-controlled trials reported by Linde et al (118; 5–1270).

An example of some of the key issues can be taken from the two studies that have examined the effectiveness of homeopathy in otitis media in children. In the first of these papers, more patients on homeopathy than those on standard care were found to have a normal tympanogram after a treatment period of 12 months. The second article reported decreased symptom scores in acute otitis media after 24 and 64 h in patients receiving homeopathy compared with those given placebo. These were the only statistically significant effects observed in either investigation. Both studies were preliminary in nature and had small sample sizes—33 and 75 patients, respectively. Both study designs involved randomisation of patients, but of course the comparative trial was not double-blinded. The intrinsic quality of these studies is higher than average in the homeopathic research literature.

Balance of research evidence
The above caveats (low volume, publication bias, low quality) are important in considering the research evidence base of homeopathy. Nevertheless, positive effects of homeopathic treatment are apparent in 50 published trials (over half of the included research literature). This represents a body of research where, for at least one outcome measure per trial, the Null hypothesis has been rejected in favour of homeopathy. Three of the papers (in otitis media, osteoarthritis and back pain) provide research evidence that homeopathy can actually be superior to conventional treatment. Only two trials have found homeopathy to have less effect than placebo.

Based on the relative number of placebo-controlled studies with positive results, the balance of research evidence currently favours homeopathy in childhood diarrhoea, fibrositis, hayfever, influenza, pain, side-effects of radio-/chemotherapy, sprains and upper respiratory tract infection. Based on published research to date, it seems unlikely that homeopathy is efficacious for headache, stroke or warts.

Insufficient research in 20 medical conditions prevents clear conclusions from being drawn. There has been no research at all in homeopathy for many other ailments. It is thus not surprising that comprehensive meta-analyses or systematic reviews in homeopathy have not discerned any clear pattern of medical conditions that appear especially promising for effective homeopathic intervention. Meanwhile, homeopathic practitioners continue to chronicle their successful clinical cases.

Future opportunities and direction in homeopathic research
Key issues that must be addressed in future research development in homeopathy include: the research question, the associated trial design and the outcome measures chosen. Fresh research should consider carefully whether placebo-controlled trials and physical determinants of health are necessarily the wisest approach. Such approaches may be particularly inappropriate in researching homeopathy for chronic illness or where the treatment does not address a named disease. Conditions of this nature are nearly always treated by individualised homeopathy, where remedy selection is based on a person’s ‘constitutional’ character, and so non-placebo-controlled designs using ‘quality of life’ measures, for example, might be the most relevant. The most appropriate place for placebo-controlled trials in homeopathy might be in examining acute (as opposed to chronic) medical conditions, where any homeopathic treatment effect is likely to be swift acting, and thus better discernable. The fact that prescribing is relatively simple (minimal range of indicated remedies) in some acute conditions could offer useful advantages in study design. It may be noteworthy that acute, rather than chronic, conditions feature prominently among those for which homeopathy has the greatest weight of positive research evidence in placebo-controlled trials.

Investigators might also consider testing the effects of homeopathy as an adjunct to conventional medication, thus reflecting its complementary nature. Equivalence trials offer another promising way forward. In these, a conclusion of ‘similar clinical outcome’ between homeopathy and an orthodox treatment would be based on an ability to accept statistically equivalent confidence intervals in the two groups of data. This approach would be greatly preferable to assuming equivalence based merely on failure to reject the Null hypothesis in a typical superiority trial, as is the case in nearly all of the 41 examples presented here. Formal equivalence trials could enable researchers to examine more robustly the relative safety and cost-effectiveness of homeopathy compared with a conventional medicine that was shown to possess similar treatment effectiveness in a particular clinical situation.

It remains to be seen whether passage of time sees the publication of increased numbers and quality of published research papers relevant to homeopathy that report clinically significant findings in its favour. For its practitioners, such robust research data would have an important impact in improving the credibility as well as the intrinsic quality of the homeopathy that they provide to their patients.

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