The best studies show individualised homeopathic treatment has beneficial effects beyond placebo

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Several systematic reviews and meta-analyses of homeopathy have been performed. However, none had looked solely at placebo-controlled trials of individualised homeopathic treatment as delivered by homeopaths in practice. The research team of Mathie et al.1 have now performed such an analysis and found that homeopathic medicines, when prescribed during individualised treatment, are 1.5- to 2-times more likely to have a beneficial effect than placebo. Use of a rigorous and transparent methodology, including a sensitivity analysis, gives credibility to these findings, which fundamentally challenge claims that homeopathy is purely a placebo effect.

**Introduction**
To date, many of the systematic reviews of clinical studies on homeopathy have analysed studies on all forms of homeopathic treatment together, in an attempt to answer the general question, “Is homeopathy better than placebo?” However, homeopathy takes several forms. Individualised homeopathic treatment, consisting of a consultation plus personalised prescription, is considered to be usual care as provided by homeopaths in real world clinics. In contrast, non-individualised homeopathy involves the same remedy being used by all patients, based on a clinical diagnosis only (e.g. over-the-counter homeopathic preparations containing multiple remedies for conditions such as hay fever or travel sickness).

There is no reason to assume that different homeopathic treatment approaches are equally effective or ineffective. It is therefore not surprising that studies combining the results of all homeopathy trials, with little or no attempt to disentangle the different types of treatment involved, have led to some negative studies and reports2-3 and ensuing heated debate. In Mathie et al’s study, placebo-controlled trials of individualised homeopathic have been analysed in isolation, allowing us to explore the key question - do homeopathic medicines, when prescribed during individualised homeopathic treatment (IHT) have an effect beyond placebo?

**Meta-analysis of Individualised Homeopathic Treatment (IHT)**
Mathie et al.1 identified 22 eligible clinical trials comparing Individualised Homeopathic Treatment (IHT) to placebo for a range of clinical conditions. To ensure that the results would be recognised by the wider academic world, Mathie et al. used state-of-the-art methods for analysing a large body of clinical trial data; namely a systematic review and meta-analysis (see Definition box).

All 22 trials were assessed for quality using the well-recognised Cochrane collaboration’s assessment tool4 and given an overall “reliability” rating of A, B or C. Three of the 22 trials met the strict criteria set by Mathie et al. to be designated as the most “reliable” evidence (i.e. rated B1 and above); meta-analysis of these three top trials found that IHT is more beneficial than placebo. It is important to note that this definition of “reliable” is more stringent than that used in previous meta-analyses of homeopathy performed by other groups (e.g. Shang et al5). Also, this method of classifying study quality and “reliability” should not be misinterpreted as suggesting that the remaining 19 trials are not meaningful. Rather, they are simply lower down the scale of relative reliability.

**Key findings**
Overall, IHT had a positive effect that was statistically different from placebo. Specifically, individually prescribed homeopathic medicines were found to be 1.5- to 2-times more likely to have a beneficial effect than placebo. The size of the treatment effect was measured by the ‘Odds Ratio’ (OR), if an OR is greater than 1.0, the effect of the intervention is positive, and the greater the OR, the greater the size of that positive effect.

The treatment effect seen in the 3 trials designated as most “reliable” was calculated to be OR=1.98 (95% CI [1.16 - 3.38]; p < 0.01) As these results were based on only 3 studies, Mathie et al. performed a ‘sensitivity analysis’ to check that they were robust i.e. the choice of trials analysed was changed in multiple ways according to their quality rating to see whether this caused the final result to alter (see Figure 1).

When analysing the 12 trials rated as B6 and above, the OR did not change significantly: OR=1.63 (95% CI [1.24 - 2.14]; p < 0.001) (Fig. 1 All studies). This sensitivity analysis demonstrates that Mathie et al.’s findings are robust. It is also important to note that there is no evidence of larger treatment effects being found in lower-quality trials, contradicting the notion that only poor quality studies on homeopathy show positive results.

![Figure 1](https://example.com/figure1.png)

**Figure 1**: Sensitivity analysis. Meta-analysis results for various sub-groups of the 22 eligible trials. Each line represents a different sub-group of trials according to their quality/reliability rating (B1 being the lowest and B6 the highest). The top line (“All studies”) represents the odds ratio (OR) results from all 22 studies pooled together. Successive lines from top to bottom represent the results after step-wise removal of trials with the next reliability rating. The bottom line (“B1 Reliable studies only”) represents the results when analysing the three best trials only. (Figure reproduced with permission from Mathie et al.1)
When testing the efficacy of IHT for several different clinical conditions, one might expect the results to vary depending on the condition being treated, making it more difficult to detect a specific effect when all conditions are pooled. Interestingly, this was no the case. Additionally, two of the three most ‘reliable’ trials used homoeopathic remedies that were diluted beyond the Avogadro limit, yet a significant specific effect was still detected. This is a striking finding considering that many detractors of homoeopathy argue that this is either scientifically implausible or simply impossible.

While the effect of individually prescribed homeopathic medicines was greater than placebo, the clinical ‘effect size’ detected was ‘small’. To put this into context, conventional drugs with a similar effect size include sumatripan for migraine, fluoxetine for major depressive disorder and cholinesterase inhibitors for dementia.

Comparison with other studies

Two previous systematic reviews of IHT have been performed. Ernst et al (published in 1999) located 3 randomised controlled trials comparing IHT to conventional medicine and the low trial quality prevented any conclusions from being drawn. In 1998 Lindel et al’s study looked at 32 trials of IHT versus placebo and found a positive, but unconvincing, trend. Mathie et al added an extra level of significance to these previous systematic reviews by performing a state-of-the-art meta-analysis.

When the meta-analysis of Mathie et al. is directly compared with perhaps the most often cited meta-analysis of “global” homoeopathy performed by Shang et al., which reached negative conclusions, key differences between the two studies become clear:

- the criteria for reliability of the clinical trials used by Mathie et al were more stringent
- the trials used by Mathie et al were more up-to-date (12 of the 22 trials identified were not included in Shang et al., published in 2005)
- the positive results of this study are based on trials which test individualised homeopathic care; Shang et al’s final conclusion that homoeopathy does not have an effect beyond placebo was based only on trials of non-individualised homeopathy
- Mathie et al performed a rigorous sensitivity analysis to confirm that despite basing their main conclusion on only 3 of 22 available studies, the findings are reliable. Shang et al. did not perform such an analysis on their data, but other authors have shown that their results (based on only 8 of 110 available studies) fail a rigorous sensitivity analysis and are therefore unreliable.

Impact of the study

In summary, Mathie et al have taken the three most reliable, high quality studies of individualised homeopathic treatment available and found that when the results are analysed together, the result is positive, showing a beneficial effect of homeopathic medicines beyond placebo. The input from two highly respected, independent biostatisticians from the University of Glasgow as co-authors gives further credibility to the findings.

Although the authors remain only cautiously optimistic about their findings, the meta-analysis by Mathie et al is well constructed and methodologically sound, providing a strong argument in favour of the existence of specific effects beyond placebo in real-world homeopathic treatment. The results of this meta-analysis challenge the commonly repeated argument, ‘the best studies show homeopathy doesn’t work’, and provide strong evidence that the opposite is actually correct, i.e. the best studies show homeopathy works.

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References