

Homeopathy on trial - The need for targeted research into specific medical conditions

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This edition of the HRI quarterly research article focuses on how discussion of the evidence base has evolved in recent years and the implications this has for the HRI's research strategy.

Introduction

When discussing the evidence for homeopathy, one quickly notices how often we are asked, 'What is your best trial? Just show me one good trial!' There are of course many types of trials which are widely accepted and routinely used to test both conventional medicine and homeopathy, but further conversation quickly determines that in fact what people are actually asking for is something very specific; they are actually only interested in one thing - a 'large', double-blind randomised placebo-controlled clinical trial ('RCT'), often purported to be the 'gold-standard' of research trials.

Interestingly, this request comes most frequently from those well-versed in research, including academics, doctors and health policy makers, who usually follow the well-established Evidence Based Medicine approach. This convention places systematic reviews and meta-analyses (studies analysing the results of multiple trials) at the top of the evidence hierarchy, not single RCTs. So, why are they not asking about the reviews and meta-analyses assessing the whole evidence base? And to answer their question, what is our 'best trial'?

20 years of debating the data

Between 1991 and 2005, the five major systematic reviews were carried out, attempting to collectively analyse the findings of all RCTs carried out in homeopathy. Accurate interpretation of these studies continues to be hotly debated¹. Those who have an a priori belief that homeopathy can be efficacious state that four of these reviews are positive i.e. showing that homeopathy does have an effect beyond placebo²⁻⁵ and one is negative i.e. concluding that homeopathy does not have an effect beyond placebo (Shang et al, 2005)⁶, meanwhile those who have an a priori belief that homeopathy cannot work because it is scientifically implausible, state that all four of the positive reviews are flawed, the only reliable study is by Shang et al., and that this study shows definitively that homeopathy has no effect beyond placebo. Such has been the impasse since 2005.

How reliable is Shang et al. in 2013?

To this day, detractors continue to dismiss homeopathy as nothing more than placebo, whether in the scientific literature, media or Government, based almost entirely on

Shang *et al.* So, if people are confident to write off an entire system medicine due to the findings of one study, surely this must be a 'bullet-proof' piece of research?

In fact, multiple concerns have been raised about the Shang *et al.* study, particularly the fact that its conclusions were based on only 8 out of the 110 identified by the authors at the time and that it fails a sensitivity analysis⁷, i.e. if you remove just one of the 8 trials they used in the analysis, the result is reversed, showing that homeopathy works beyond placebo.

But reliability of the analysis is not the only problem with the Shang paper. As we take a fresh look at the evidence in 2013, we also need to consider how well this study reflects the entirety of today's evidence base. A recent literature search by Mathie *et al.*⁸ has identified 151 placebo-controlled randomised trials which would have met the inclusion criteria for Shang's review - 41 more than identified in 2005. This demonstrates the extent to which this 8 year old review, which now covers only 73% of the eligible trials, has become outdated.

Homeopathy research evolves and matures

Until recently there was no concept of whether the homeopathic treatment provided within a trial was appropriate or not. Indeed, what meaning does a negative result have if the homeopathic treatment used would be considered by peers to be poor quality? To make an analogy with conventional medicine, how much meaning would anyone give to the results of a trial which set out to assess whether antibiotics can treat migraine? Robert Mathie and colleagues have recently published a paper on this topic⁹, introducing the concept of 'model validity' and ways to analyse this aspect of trial quality. This will change how we assess the evidence base we already have and inform future trials.

Homeopathy's 'best evidence' for a single condition

In any system of medicine, one would expect some clinical trials to be positive and others to be negative, mapping out areas where treatments are useful and areas where they are not. So, the question is not so much about counting the total number of positive versus negative trials in homeopathy, as has so often been done in the past, but to ask, "What is the best evidence that homeopathy can treat even a single medically relevant condition".

When looking at this question we can identify a number of clinical conditions where the research shows a clear trend in favour of homeopathy¹⁰. For example, the Cochrane review of homeopathy for the treatment and prevention of flu, shows that homeopathy is indeed able to treat flu ($p=0.001$), though not prevent it¹¹. One should also mention a meta-analysis of three placebo-controlled randomised trials involving a total of 242 children, which showed that individualised homeopathic treatment reduced the duration of acute diarrhoea ($P=0.008$)¹³.

The broadest evidence base relates to upper respiratory tract infections, where the consensus from some 29 trials (26 of which were positive) is that homeopathy is effective for conditions such as ear infections (acute otitis media, sinusitis and pharyngitis)¹².

Acute otitis media (AOM) is of particular clinical relevance in the UK, as it is among the commonest causes of children being brought to medical attention and the Department of Health is aiming to reduce inappropriate prescription of antibiotics for this condition¹⁵. Coupled with this, the existing research evidence is highly promising with eight positive studies^{12,16,17}. Most recently an Indian team conducted a pilot study comparing individualised homeopathy with conventional care in 81 children suffering from AOM¹⁷. In the conventional group, all 40 patients (100%) were cured. In the homeopathy group, 38 patients (95%) were cured while 2 patients (5%) were lost to the last two follow-up. The authors concluded that individualised homeopathy is an effective conventional treatment in AOM, as there were no significant differences between groups.

When looking for our 'best trials' for homeopathy in a specific medical condition, it's also interesting to look at veterinary research. In an industrial farming setting, researchers in the Netherlands carried out an observer-blind, randomised placebo-controlled trial to assess the efficacy of homeopathic medicine *Coli 30K* in prevention of *E. Coli* diarrhoea in neonatal piglets. The results clearly showed an effect of the homeopathic medicine with only 3.8% of the homeopathy group suffering from diarrhoea compared to 23.8% in the control group ($p<0.0001$)¹⁴. This is of particular interest when one considers that the medicine used was a so called 'ultra-high dilution' which should not contain any molecules.

HRI's research strategy

What we can say right now is that the trials described above are some of our 'best trials'. They are high quality, suitably blinded, randomised, placebo-controlled trials and they are positive. However, to provide definitive evidence acceptable to decision-makers, more research is needed.

When one considers the general scarcity of research funding in homeopathy it is vital that resources be targeted to areas with maximal potential impact. In practical terms this means targeting common 'effectiveness gap' conditions for which conventional treatments are unsatisfactory. HRI is currently providing financial and/or academic support to a range of projects which meet these criteria e.g. attention deficit hyperactivity disorder (ADHD), depression and irritable bowel syndrome (IBS). For the reasons outlined above, childhood ear infections - aka acute otitis media - is an additional target for our future efforts.

Moving beyond the controversy

Homeopathy will remain controversial until either its mechanism of action is understood or the body of evidence showing that homeopathy works for a specific clinical condition becomes indisputable. HRI is working with experts worldwide to promote research in both these directions, but answering the question, 'What can homeopathy treat?' is more immediately relevant to patients and clinicians and perhaps a more rapidly achievable goal.

What is emerging is the idea that it makes little sense to continue to put a whole system of medicine on trial by point-scoring; what does make sense is to concentrate our research efforts on a small number of the most promising clinical areas. Furthermore, if we can open up discussion between those on both sides of the debate to clarify the most appropriate research questions and trial designs before projects commence, then generating meaningful results - able to resolve the current impasse - becomes a realistic possibility.

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