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Homeopathy and the Question of Evidence Base

The recent catch-phrase in conventional medicine is "evidence base". Doctors are taking it upon themselves to use only drugs that, through carefully controlled research, have proved efficacious to the condition treated. The "gold standard" for such research is the Randomized Control Trial (RCT), which allows researchers to differentiate between placebo effect and a genuine therapeutic effect of the drug.

Whilst many conventional treatments are not yet supported by RCT's[1], homeopathy is now expected to be measured by the same standard. This expectation is partially why homeopathy has received so much bad press recently. Unfortunately, bad press has practical results: NHS health commissioners can now confidently state that "homeopathy is not evidence based".[2]

To what extent is this claim true? What is the evidence base for homeopathy?

It is quite rare to find truly unbiased studies of homeopathy. Whilst homeopaths might be over-zealous to supply positive results, other researchers see homeopathy a-priori as scientifically impossible. In the following review I have tried to use, as much as possible, studies that seem to start from a neutral point of view. Among studies with positive results I have ignored, or clearly qualified, work whose results were not corroborated by further research.

Homeopathy's mechanism of action

The most contentious claim made by homeopathy is that ultra-diluted substances can have a clinical effect. The suggestion that remedies diluted beyond Avogadro's number can be active certainly "contradicts high-school level chemistry"[3], and is difficult to assimilate by doctors and homeopaths alike. There are currently some alternative theoretical models regarding homeopathy's mechanism of action[4]. These models rely on applications of chaos theory and quantum physics[5,6], or on cutting-edge material theories[7,8]and are mostly speculative. Whether these, or any other explanation, would generate more support, remains to be seen.

Notwithstanding the need for a coherent explanatory theory, we must bear in mind that lack of such an explanation is not a rational reason to reject the hypothesis that homeopathy is effective. After all, it took decades, for example, to understand how aspirin works, yet this gap did not infringe on its perceived efficacy[9].

Efficacy-based research may be divided to pre-clinical, or clinical. The amount of pre-clinical research in homeopathy is small, and, obviously, it does not translate automatically into clinical efficacy. It can, however demonstrate that, contrary to what a

chemist would expect, homeopathic remedies are active agents. Following are some examples:

Linde et al[10] published in *The Lancet* a critical meta-analysis[1] of detoxification experiments, checking the power of homeopathic remedies to reverse toxological effects on plants and animals. They found that in high-quality experiments positive results were twice as likely as negative results. Such research suggests that homeopathic remedies are active substances, when compared to untreated substances.

Some researchers tried to check whether homeopathic dilution and succussion would change the physico-chemical properties of the solvent, with positive results[11,12]. Others have demonstrated that homeopathic remedies have measurable effects on animals. Eg Datta et al[13] found that the homeopathic remedy Arsenicum Album was effective in countering the effects of arsenic poisoning in rats. There are quite a few similar studies with positive results[2]. Furthermore, homeopathic remedies are effective in treating cells in vitro, eg when ultra-diluted histamine modifies basophile behaviour[14,15].

Researching clinical efficacy

Research into the clinical efficacy of homeopathy is generally reliant on either Randomized Controlled Trials (RCTs), where homeopathy often struggles to demonstrate efficacy, or on outcome studies, where it is practically always successful. We'll consider each of these in turn.

Some RCT-based studies into the clinical effects of homeopathy fail to demonstrate that homeopathy is better than placebo. But a closer look reveals complex methodological problems in the application of RCTs to homeopathy[2,16,17,18]. Possibly due to these methodological inadequacies, homeopathy often fails to demonstrate results better than placebo, even if it does bring about a valid clinical effect, beyond regression to the mean[8,19].

There a few possible reasons for this phenomenon:

1. RCTs are designed to isolate the drug's effect from all other effects. This ability – to differentiate the specific effect from the non-specific - is what makes this method the gold standard of medical research. But unlike chemical drugs which target a specific tissue, hence can demonstrate a specific effect, homeopathy operates indirectly, **through stimulating the body's healing mechanisms**, "Thus, [its] way of achieving efficacy is non-specific" [8,15,20].

2. Homeopathy, being a holistic intervention, examines the whole being rather than the presenting symptom; thus, **homeopathy's effects manifest not only on the presenting physical complaint**. Rather, homeopathy also affects secondary physical symptoms, emotional symptoms and general symptoms, such as wellbeing. These outcomes would

[1] Meta-analysis is a study that collects the results of similar previous studies – often with conflicting results – and aims, through statistical means, to arrive at one, definite, conclusion.

be considered, under most study designs, as non-specific, or placebo effects. Hence, such effects would be ignored in most studies, even if their importance to the patient's quality of life is noticeable[16].

3. Apart from its generalized healing, homeopathy also induces **other non-specific effects**. A homeopathic consultation is often emotionally-involved, exposing the disharmonies in patients' lives. Some suggest that even without receiving a remedy patients would derive extra benefit from the mere consultation, over and above conventional treatment[16,21].

4. Furthermore, it is practically impossible to design RCT studies for complex intervention such as homeopathy **that would preclude any interference between the different arms of the study**[22]. This, again, reduces the chance of demonstrating an effect over and above placebo.

Notwithstanding the above-mentioned problems, some high quality RCT meta-analyses and reviews have shown evidence positive to homeopathy[23]. For example, Kleijnen et al in a BMJ article[24] performed a detailed evaluation of 107 homeopathic clinical trials, finally using 60 trials of high quality, and concluded that they "would be ready to accept that homeopathy can be efficacious, if only the mechanism of action were more plausible."

Putting the clinical research into perspective

Taking the inherent difficulty in RCT into account, it is not surprising that some researchers relying on this method, such as Shang et al[25] in a recent *Lancet* article, judged homeopathy negatively. This article, which received wide exposure, was a meta-analysis comparing clinical results from symptom-specific RCTs. The authors concluded that homeopathy is no better than placebo. However, over and above the basic methodological difficulties mentioned above, this article is deeply flawed in fundamental ways. For example, the researchers chose only 8 out of 110 papers about homeopathy, without disclosing which papers where rejected and why. Furthermore, the chosen papers were not appraised for their external validity (ie, the real clinical effect), but only for their internal validity (how stringent were randomisation and control). Fisher[26], says that this article "fails, on multiple counts, to meet the generally accepted standards for meta-analysis—the QUOROM statement (Quality of Reports of Meta-Analyses of Randomised Controlled Trials), published in *The Lancet* itself in 1999". Such flaws would not have gone unnoticed if it the paper was endorsing homeopathy, reflecting a publication bias against the discipline[2,27,28].

Homeopathy's chances to fend for itself are limited: there are the inherent methodological difficulties described above, a dire lack of funding compared to mainstream research, a publication bias against positive papers in peer-reviewed journals[29] and a conceptual bias due to homeopathy's debatable mechanism of action[27]. Given all of the above, the fact that homeopathy has managed to drum up any research support at all stands witness to the discipline's efficacy.

Outcome-based research

Apart from RCTs, it is also possible to use outcome studies as evidence to homeopathy's effectiveness. Such research has its own methodological limitations, primarily the patient's awareness of the researcher's expectations. Notwithstanding this difficulty, results from such research are overwhelmingly supportive of homeopathy[30,31].

Recently, Spence, Thompson and Barron[32] conducted such study in the Bristol Homeopathic Hospital. The sample included a total of 6544 follow-up consultations given to patients who were referred by GPs due to chronic conditions. The authors found that 70.7% of patients (n = 4627) reported positive health changes, with 50.7% (n = 3318) recording their improvement as better (+2) or much better (+3), using a 7-point scale.

In fact, not only does outcome studies show that homeopathy is effective in clinical studies, it also shows that in chronic conditions it can be more effective than conventional medicine[33,34]. Yet most conventional treatments have shown to be clearly better than placebo, a feat which homeopathy struggles to achieve. There is a paradox here, which goes back to our discussion of methodological difficulties, and will probably take many years to resolve.

Summary

We witness an increased demand for homeopathy from the public, accompanied by a popular perception that patients are satisfied with the treatment. Yet the evidence that homeopathy is better than placebo is inconclusive. Consequently, one of the best critical reviews of homeopathy maintains that: "the **system of homeopathy** may be more beneficial in actual practice than when studying the **isolated remedies themselves**"[27]. Other researchers concur, saying that we must "redirect our energies to analyses of **whole-systems healthcare**"[21]. And that "It seems more important to **define if homeopathists can genuinely control patients' symptoms** and less relevant to have concerns about whether this is due to a 'genuine' effect or to influencing the placebo response."[35].

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