Appendices to Submission

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Appendix 1
The submission of the

AUSTRALIAN HOMŒOPATHIC ASSOCIATION INC.

to the

National Health & Medical Research Council:

review of the evidence towards the development of a

position statement on Homoeopathy.

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Executive Summary

This paper presents an introduction to homoeopathy and the controversial matter of ultra-molecular medicines used in homoeopathy. An overview of research in homoeopathy is presented. The paper identifies positive findings for homoeopathic treatment in some randomised controlled trials, details positive findings in four out of five comprehensive systematic reviews of homoeopathic research and describes the compellingly positive data derived from observational studies of homoeopathic treatment at a population level. Homoeopathy is a complex health care intervention and the challenges of research in this field are discussed.

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*The Australian Homoeopathic Association (AHA) is the national peak body representing the homoeopathic profession in Australia. The AHA is active in advancing the capacity of its members in their role as health care professionals. The homoeopathic profession was the first of the Complementary and Alternative Medicine (CAM) professions to develop government-endorsed National Competency Standards for education. Since 1999, the Australian Register of Homoeopaths ([www.aroh.com.au](http://www.aroh.com.au)) has provided a framework for professional standards and the accreditation of educational courses, and has facilitated communication between the profession, government and the public. All AROH-registered homœopaths meet the competency standards established by the profession and endorsed by the Federal Government. They also meet the criteria for ‘recognised professional’ recommended in the 2003 Government report: “Expert Committee on Complementary Medicines in the Health System”. These criteria were subsequently endorsed by the Federal Government in their 2005 response to the Expert Committee’s report. AROH-registered practitioners are bound by a Code of Professional Conduct, have current indemnity insurance, are required to engage in continuing professional education, and possess current Senior First Aid certification. All AHA professional members are registered with AROH.*
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The Australian Homoeopathic Association (AHA) invites the interest of the NH&MRC in the practice of homoeopathy in Australia. We trust that the inquiry by the NH&MRC signals an era of cooperative investigation into the highly valuable but under-researched medical modality of homoeopathy.

We note that no formal terms of reference apply to the NH&MRC inquiry into homoeopathy. The AHA takes the initiative in putting the following material before the NH&MRC in four parts: the context of the inquiry, a brief outline of homoeopathy, the issue of medicinal ultra-dilutions and an overview of clinical research in homoeopathy.

1. The context of the NH&MRC review.

The present review by the NH&MRC takes place at a time of continuing growth in the use of complementary and alternative medicine (CAM) in Australia. This phenomenon has stimulated many academic researches into this consumer-led trend in health care (Xue, Zhang, Lin & Story, 2006; Xue, Zhang, Lin, Da Costa & Story, 2007; Xue, Zhang, Lin, Myers, Polus & Story, 2008; Zhang, Xue, Lin & Story, 2007).

The NH&MRC will be aware that research bodies have been established to address community demand for greater research into CAM approaches in health care, such as the National Institute for Complementary Medicine (NICM). The establishment of NICM followed the recommendation in 2003
of the Expert Committee on Complementary Medicines in the Australian Health System: the expert committee advised that government has a social responsibility to fund complementary medicine research given the high community use of complementary medicines and therapies.

While Australia is internationally renowned for the strength of its medical research, it provides one of the lowest levels of research investment in CAM therapies. This is despite the fact that Australia has one of the highest levels of use of complementary medicine per capita in developed nations: two out of three Australians have used complementary medicines in 2010-2011 (www.nicm.edu.au). In the present environment, where growing health care costs are of increasing concern in an ageing population, it is of interest that NICM has recently released the results of a study demonstrating the relative value of complementary medicine interventions to the community. This study, conducted by Access Economics (www.nicm.edu.au/content/view/174/295), has found that millions of health care dollars could be saved without compromising patient outcomes if complementary medicine was more widely used.

It is proper therefore that the NH&MRC, Australia’s peak body in health research, should not merely evaluate research currently available but commit its resources to further research into CAM therapies and so assist Australian consumers to make well-informed health care choices: respecting the autonomy of consumers and advancing these choices. Of the range of CAM interventions in community use, homoeopathy should attract the interest of health researchers and health economists alike given the benefits of homoeopathic medicines in terms of relative safety (Adler, 1999; Bornhoft
et al, 2006; Dantas & Rampes, 2000; Thompson, 2004) and the modest and comparatively much lower costs (Christie & Ward, 1996; Jain, 2003; Swayne, 1992) of its medicines. Low environmental impacts may also be anticipated from the sourcing, research in and manufacture of these medicines, relative to other pharmaceutical products: this research remains to be done.

The AHA notes that the promotion of ethical standards in relation to patient care, public health and health research is a current objective of the NH&MRC (Objective 4 of the 2010-2012 NH&MRC Strategic Plan). The AHA is therefore confident that the NH&MRC will conduct its investigations into homoeopathy in a comprehensive, just and fair manner. The homoeopathic community of practitioners and patients relies on the NH&MRC to draw broadly and enquire deeply of all of the resources and research material available in carrying out its important task of protecting and promoting community health – well guided by the values of autonomy, justice, beneficence and non-maleficence (Beauchamp & Childress, 2001).

It is in this context that the AHA cautions the NH&MRC against any over-reliance on the findings of the U.K. House of Commons Science and Technology Committee Evidence Check 2: Homoeopathy – Fourth Report of Session 2009-10 (House of Commons, 2010). The NH&MRC will be aware that the recommendations of the Science and Technology Committee (STC) - to restrict the availability of homoeopathy through the National Health Service - were not endorsed by the U.K. Parliament. Parliament decided that to do so would be illiberal and that decisions about health care
were best made between patient and doctor. In its response to the issue of patient choice, the government noted that:

“The department of health wholly supports the concept of the informed patient. The informed patient is better placed to be able to make decisions about their care and well-being and better equipped to manage changes in their health status” (U.K. Government Response to the STC report, paragraph 17).

The autonomy of clinicians was also supported by the following comment:

“It is not appropriate for the Department of Health to remove the right of (Primary Care Trusts) to make these (decisions regarding patient care) on a case-by-case basis” (U.K. Government Response to the STC report, paragraph 33).

It will be of concern to a respected organization such as the NH&MRC that the proceedings of the House of Commons Science and Technology Committee Evidence Check 2: Homoeopathy have been subject to several serious criticisms which must limit the reliability of the inquiry and its findings. These criticisms included concern about its selection of committee members, the protocols engaged in its meetings and hearings, limited time and notification of its oral hearings, a perceived bias in its appraisal of the evidence before it, and the very restricted number of committee members who ultimately passed its recommendations. We draw your attention to documents which detail these concerns, produced by the U.K. Society of Homoeopaths (www.homeopathy-soh.org), by Earl Edward Baldwin (British Research Council for Complementary Medicine (1989-91), British Acupuncture Accreditation Board, 1990-98; see www.britishhomeopathic.org/research/science_science_and_technology_co
mmittee_report.html), and by William Alderson, the chairperson of Homoeopathy: Medicine for the 21st Century (www.homeopathyworldcommunity.com). The British Homeopathic Association makes a particularly pithy assessment of the STC:

“Far from being a "report by experts" as bandied in the press, only three committee members out of a possible 13 passed the report, none of the three has any knowledge of homeopathy and all of them have failed to be re-elected to parliament. The report was negatively biased in its findings and recommendations and... evidence gathering was riddled by poor process. The report did not adequately acknowledge the factual research evidence and dismissed the patient outcome studies in favour of homeopathy. (www.britishhomeopathic.org).

In their formal reply to the recommendations of the report, the British Homoeopathic Association wrote that the review was:

“systematic only in excluding facts that tend to support homoeopathy: it omits or misrepresents any research evidence which challenges the view that a patient’s response to homeopathy is due to placebo. Its conclusions are unsustainable in the light of scientific evidence.”
http://www.facultyofhomeopathy.org

The critical issue of clinical evidence for homoeopathy and the findings of the STC in relation to this evidence will be discussed at length later in this document.
It is the hope of the AHA that in light of the material presented below and
the NH&MRC’s own further inquiries, the Council’s review will result in
greater research interest in Australia in the field of homoeopathic medicine.
This area of medical science has to date received relatively limited research
attention: however its rich literature recording an enduring clinical history,
along with such contemporary research as is currently available, may
demonstrate to the open-minded inquirer that homoeopathy has the potential
to make further, highly valuable contributions to community health care.

2. Homoeopathy

Homoeopathy has a two hundred year worldwide history of clinical
practice: homoeopathy is practised in 41 out of 42 European countries
(ENHR, 2006), in the Americas and the Indian sub-continent (Medhurst,
2004). In many instances homoeopathy forms an integral part of national
health programs. The World Health Organisation promotes the
“endorsement, integration and evaluation” of traditional medicine
(www.who.int/medicines/technical_briefing/tbs/Technical_briefing_11_10
pdf) and recognises homoeopathy as the second most widely practised
health care modality worldwide after Traditional Chinese Medicine.
Reviewed globally, homoeopathy is most commonly practised by
conventionally trained medical doctors, using this modality in conjunction with other treatment choices. In Australia there is a small cohort of medically trained homoeopaths (The Australian Medical Faculty of Homoeopathy), while the majority of Australian homoeopathic practitioners operate within the complementary and alternative medicine (CAM) sector.

Throughout the history of homoeopathy and up to the present, a substantial body of literature has attested to its widespread clinical application and detailed its theory and method. Classical homoeopathy diagnoses and treats illness from within its paradigm of holism (Gerber, 1988): a gestalt or concept of the unity of the physical and psychological state of the patient is at the heart of the homoeopathic approach. Theories describing psycho-neuro-immunological (PNI) approaches to health (Diodge, 2007; Oschman, 2000, 2002, 2003, 2006, 2008) provide contemporary iterations of a unitary conception of health and disease, such as is found in homoeopathy. The consistency of this approach over many generations of clinicians in homoeopathy has fostered an accretion of knowledge of this therapeutic approach. Professional journals on every continent where homoeopathy has been practised provide a continuous record of its use, and detail hundreds of thousands of homoeopathic case studies. The range and quality of journals serving the homoeopathic profession flourishes in the present decade, and are witness to an acceleration of knowledge in this field.
Homoeopathic literature chronicals the evolving body of empirical clinical experience of its practice. Through this record of use, the knowledge base of homoeopathy has grown and developed, it has contributed to the education of practitioners and fostered the growth of the discipline. While this long-standing and widespread record of clinical use may fall short of contemporary measures of proof, an exploration within the richly recorded history of homoeopathy and into the dynamism of its contemporary practice would invite the serious inquiry of the truly scientifically curious.

The founder of homoeopathy Dr. Samuel Hahnemann (1755-1843) was an avidly curious scientist who applied an experimental approach to his professions of medicine and pharmacy by testing the effects of medicinal substances on healthy human subjects (homoeopathic ‘provings’) (Dean, 2004). From his clinical application of these medicines, the concepts, theory and method of homoeopathy evolved and the homoeopathic materia medica (HMM) developed. Additions and refinements to the homoeopathic pharmacopoeia were made throughout Hahnemann’s life and continued through the nineteenth and twentieth centuries (Aulas & Chefdeville, 1984). Re-provings of original medicines have up-dated knowledge of these medicines (Dantas & Fisher, 1998; Fuller-Royal, 1991; Riley, 1994; Sherr, 2009; Walach, 1993, 1998) and new medicines are proven: some of them sourced from indigenous substances by Australian homoeopathic researchers (Gray, 2005a,b, 2006a,b; Marks & Twohig, 2000).
Contemporary writings on mineral medicines (Le Roux, 2005; Morrison, 2009; Sankaran, 1996, 2008; Scholten, 1993, 1996, 2006; Shah, 2010; Tuminello, 2005), on the plant families (Sankaran, 2004a, 2004b; 2007; Sankaran & Boldota, 2008; Vermeulen, 2007) and on animal-derived medicines (Bailey, 2010; Hatherly, 2010; Herrick, 2010; Master, 2007; Sankaran & Shah, 2010; Vermeulen, 2005) describe a systematisation of the homoeopathic materia medica. In what is referred to as the ‘new’ homoeopathy (Klein, 2009), this systems approach identifies therapeutic qualities which apply to specific families of medicines (mineral, plant and animal sourced substances), and provides a methodology for the identification of specific medicines from within these groups, optimising therapeutic outcomes when these innovations are adopted.

There have been parallel developments in new and expanded presentations of materia medica over the past twenty years (Mangialavori, 2010; Vermeulen, 1992, 1994, 1996, 2000; Murphy, 1995; Vithoulkas, 2010) and likewise the ‘dictionaries’ of HMM (known as repertories) are now subject to very regular up-dates in both print and electronic formats (Schroyens, 2010; Macrepertory: www.kenthomeopathic.com/macrepertory.html; Radar: www.radar-uk.co.uk/ and others). In the same period, publications in the arena of homoeopathic methodology have flourished as psychotherapeutic approaches in homoeopathic medicine become further articulated (Bailey, 1995; Sankaran, 1994a, 1994b; 2000; Mangialavori, 2003, 2004, 2010), foundational homoeopathic approaches are reiterated
afresh (Dimitriades, 2004, 2005; Le Schepper, 2009, 2010) and existing theoretical tools are expanded (Klein, 2009).

A review of the extensive historical literature is not possible in this document and even a limited survey of contemporary works in homoeopathy is too large an undertaking. Such a resource would however be a very useful point of reference for the NH&MRC in informing its researchers and aiding its present deliberations. The AHA would be happy to assist the NH&MRC in developing this resource in the future should such an opportunity arise. Certainly many of the misapprehensions about homoeopathy appear to result from a lack of information and it is encumbent upon professional bodies to meet the need for community education wherever possible. It is an historical fact that homoeopathy has often had the effect of polarising public opinion (Coulter, 1973); in the current context, such polarities do little to facilitate commonly shared goals of improved community health care in a resource-challenged environment. It is also true that Samuel Hahnemann set his medicinal approach apart and in stark distinction from the medical practices of his day (Bradford, 2004; Haehl, 1992; Hahnemann, 1970) and that the controversies generated by homoeopathy from its inception have scarcely abated till the present time.

3 Ultra-molecular dilutions
The single most hotly and consistently contested issue is that of the serially agitated high dilutions (Lewith, Jonas & Wallach, 2002; Fisher, 2007) or homoeopathic ‘potencies’, developed by Hahnemann and in use up to the present day. Originally instituted by Hahnemann to reduce the effects of toxicity of medicines, the issue of dilution and succussion used in homoeopathy, rather than investigated, is dismissed by some quarters of the medical scientific community despite a growing body of research evidence of the effects of ultra-molecular dilutions.

Sequential dilution, with vigorous shaking at each stage of the dilution process prepares medicines in either decimal (1:10) or centesimal (1:100) series, with the original substance rendered in material quantities beyond Avogadro’s constant or in so-called ultra-molecular dilutions. The oft-remarked ‘implausibility’ of these preparations has been the focus of scientific scepticism about homoeopathy. In 1991 for instance, the BMJ stated that: “We could accept that Homoeopathy can be efficacious, if its mechanism of action were more plausible” (Kleijnen, et al, 1991). The other key tenet of homoeopathy, the principle of similarity, provokes less opposition, and is reflected in other areas of science, such as toxicology, immunotherapy and pharmacology.

It is of concern to the AHA that the U.K. House of Commons Science and Technology Committee inquiry into homoeopathy failed to take account of the evidence provided by Dr. Peter Fisher (HOC evidence 21) detailing research on ultra-dilutions. An overview of this evidence will be repeated...
here for the convenience of the present inquiry.

Dose-response anomalies were first explored by Rudolf Arndt and Hugo Schultz in the late nineteenth and early twentieth centuries, respectively. This phenomenon is now referred to as hormesis and differing theories describe the response of biological systems to low doses (Calabrese et al, 2005; 2006a,b; Calabrese et al, 2007). Pharmacology studies show drug rebound effects, dose-dependent reverse effects and paradoxical phenomena (Bond, 2001; Tiexiera 2006; Tiexeira, 2007). Biological studies have shown positive effects of ultra-molecular dilutions in high quality replicated studies (Witt et al, 2007). Other studies examine the features of substance similarity and low dose responses simultaneously and find positive effects (Weigart, 1999). Immunological studies have shown basophil activation by high dilutions of histamine (Belon et al, 2004; Chirumbolo, 2009; Devenas et al, 1988; Lorenz et al, 2003; Saint Laudy et al, 1993). Ultramolecular dilutions of aspirin have been found to have the opposite effect of substantial doses: such dilutions promote clotting (Aguejouf et al, 2008; Eizayaga et al, 2007; Lalanne, et al, 1990). Cytokine expression was shown in several studies to be stimulated by homoeopathic preparations (Betti et al, 1997; de Oliveira et al 2008; Fimiani et al 2000; Ramachandran et al, 2007; Smit et al, 2008). Laboratory experiments in animal models show the effect of ultra-molecular preparations of thyroxine, where it slows the rate of metamorphosis of frogs, an experiment replicated in different laboratories and with different species of
The so-called ‘memory of water’ effects have been established whereby previously frozen clathrate hydrate formations in water predispose later to more rapid clathrate formation (Zeng et al, 2006). The contentious ‘memory of water’ issue received considerable media attention when in 2010 the Nobel prize-winning virologist, Luc Montagnier, described that DNA produces structural changes in water which persist at very high dilutions, and that these dilutions emit measurable electromagnetic signals. Because this information was seen as reinforcement of homoeopathy from a prestigious scientist, Montagnier’s pronouncements were widely described. He responded thus:

“....I cannot say that homoeopathy is right in everything. What I can say now is that the high dilutions are right. High dilutions of something are not
nothing. They are water structures which mimic the original molecules. We find that with DNA, we cannot work at the extremely high dilutions used in homoeopathy; we cannot go further than 10 to the minus 18th dilution, or we lose the signal. But even at 10 to the minus 18th, you can calculate that there is not a single molecule of DNA left. And yet we detect a signal...” (Montagnier, 2009).

In an experimental study of ultra-high dilutions of lithium chloride and sodium chloride (Rey, 2003), emissions of light were detected in dilutions beyond Avogadro’s number (10^-30 g cm^-3). Thermoluminescence was witnessed as the solutions were irradiated by x-rays and gamma-rays at 77 K, then progressively re-warmed to room temperature. Many other studies explore the matter of ultra-molecular dilutions (Benveniste, 1981; Brach et al, 2001; Sehon & Stanley, 2003; Samal & Geckler, 2001; Jonas et al, 2006; Vallance, 1998;) and provide a variety of modes of observation and investigation into the phenomena of biological activity at these high dilutions.

Recently reported studies used electro-encephalography to monitor the brain effects of homoeopathically prepared passionflower (passiflora incarnata) and oats (avena sativa) (Dimpfel, 2010). Responses in four regions of the brain were witnessed, showing that the homoeopathic preparations elicited strong reactions similar to those of pharmaceutical drugs, confirming the results of earlier observational studies of the effects of these medicines.
Notwithstanding these studies, the therapeutic method of highly diluted, succussed medicines employed in homoeopathy confounds many onlookers and confronts the medical-scientific community with phenomena for which suitable theories are yet to evolve. In response to what is yet to be understood in science, scientific method may best be employed when used to challenge our biases, rather than confirm them. As Peter Fisher noted in his submission to the House of Commons Science and Technology Committee (HOC Evidence 21), the substantial body of work on ultra-molecular dilutions now available uses various biological models. These include research work with isolated cells, plants and animals, and demonstrate biological responses to ultra-molecular substances, with several models yielding repeatable results. The EEG study described above adds to the weight of evidence currently contesting the ‘implausibility’ argument so commonly resorted to by opponents of homoeopathy.

4. Clinical research in homoeopathy

The following table - prepared by the U.K. Society of Homoeopaths in their submission to the House of Commons STC (Evidence No 138, 143) provides a succinct outline of the range of issues confronting investigators in the field of homoeopathy:

<p>| Homeopathy is effective | Homeopathy is not effective |</p>
<table>
<thead>
<tr>
<th>Historical and case-based evidence shows the clinical effectiveness.</th>
<th>Historical and case-based evidence is not acceptable as proof of efficacy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observational studies (of which there are many) consistently report highly positive effects</td>
<td>Observational studies do not exclude the possibility that homeopathy is no more than placebo</td>
</tr>
<tr>
<td>Research methods most highly placed in the evidence hierarchy of Evidence Based Medicine (RCTs and systematic reviews) do not adapt well to complex interventions such as homeopathy</td>
<td>The only way to thoroughly test an intervention is through a placebo controlled, randomised trial</td>
</tr>
<tr>
<td>Inherent bias prevents a fair consideration of evidence such that when positive results from RCTs in homeopathy are published they are dismissed.</td>
<td>Bias exists on both sides and results can be manipulated or occur by chance</td>
</tr>
<tr>
<td>There is a distinct lack of funding available for research in homeopathy</td>
<td>Research into homeopathy should not be funded as the agents cannot be effective in the dilutions given.</td>
</tr>
</tbody>
</table>
Clinical research in homoeopathy offers the opportunity for research expositions of this method, alongside the challenge of devising suitable tools which meet both the exigencies of scientifically sound research and the complexities of this medical intervention. That research in homoeopathy is in an early stage of development is clearly reflected in the limited number of individual research papers, reviews and meta-analyses in this field. However, there is a common public misconception that no research exists in homoeopathy and this is misconception is addressed by the material presented below. The following discussion of meta-analyses, reviews and clinical trials in homoeopathy is not exhaustive: it fulfils however the purpose of detailing quality research in this field. In so doing it outlines the challenges of homoeopathic research and presents some suggestions for ways in which these may be addressed. So that the reader may gain an overview of the research situation in homoeopathy, this paper does not limit itself to the last ten years of research in homoeopathy.

Only four published papers of homoeopathic research appear prior to 1975 (Kennedy, 1971; Paterson, 1943; Ritter, 1966; Ustianowski, 1974). Growth in research has been modest: for example, in the period from 1975 to 2004, 97 published clinical trials were identified. Up until 2008, a total of 134 RCTs had been published: 59 of these (44%) were positive, 67 (50%) were neutral and 8 (6%) were negative (Fisher, 2008a). Systematic reviews have been employed to compare the results of studies, usually to establish whether homoeopathy has an effect greater than placebo. Meta-analyses
attempt the comparison of results from a number of trials sharing common objectives and methodology, so that a statistical combination and joint analysis can be undertaken. In both systematic reviews and meta-analyses, the reliability of results depends upon the similarity of the included studies, and the commonality of design and methodology. In the homoeopathic field, two factors particularly influence the viability of reviews and meta-analyses. Homoeopathy is a heterogenous modality, thus achieving commonality in the investigated material is more difficult, and the fact that researchers draw from a small number of clinical trials places further limitations on both systematic reviews and meta-analyses in this field.

Bearing these caveats in mind, the results from meta-analyses in homoeopathy have been broadly positive in finding that homoeopathy differs from placebo (Kleijnen, et al 1991; Boissel, et al, 1996; Cucherat, et al 2000; Linde, et al, 1997) until the last one published by Shang et al in The Lancet (Shang, et al 2005). This latter study will be discussed later for its singular relevance in the U.K. STC and to the current NH&MRC inquiry. However, before exploring specific research studies in homoeopathy, it is important that some of the complexities confronting such research be outlined.

4.i. Complexity and reductionism

Homoeopathy embodies an integrated approach to health and disease, which seeks to take account of the complex inter-relatedness of the biological, psychological and environmental factors characterising the individual
patient. In this approach, homoeopathy may have much in common with current developments in biomedical and molecular knowledge, which invite an account of the complex interactivity of molecules, cells, organs and systems operating horizontally (molecule to molecule) and vertically (molecule to cell, cell to organ, organ to body and body to environment) in both health maintenance and disease development (Bellavite & Signorini, 1995). The methodology employed in homoeopathic practice – extensive case-taking deriving an understanding of the unique aspects of the patient’s multi-layered expression of and response to their illness – is directed at the prescription of a single medicine based upon this individuality. It may be hypothesised that the capacity to select one single medicinal agent, closely matched to the whole state of the patient, intervenes in the homoeostatic processes of the organism in a way which reinforces those processes and so promotes equilibrium. Whatever the pathways of action of homoeopathic medicines, it is through this focus on the whole patient (rather than solely on the disease), and through the scrupulous attention given to the selection of the ‘most similar’ medicine, that homoeopathy embodies what some authors refer to as the ‘complexity paradigm’ in medicine (Bellavite & Signorini, 1995; Scholten, 2004a). These authors offer interesting conceptual discussions of homoeopathy as ‘information’ science (Bellavite & Signorini, 1995; Scholten, 2004b) and disease as a disorder of information (Bellavite & Signorini, p.85-191).

While the concept of evidence is multi-faceted, the accepted highest level of evidence in contemporary clinical research seeks to prove efficacy of one single agent in one specific disease, using the design and methodology of the randomised controlled trial (RCT). There is an inherent ‘paradigm clash’
when the ‘whole-person/whole-medicine’ approach of homoeopathy is measured within the parameters of the single disease focus of a typical drug trial. While it is clearly necessary for homoeopathy to exhibit efficacy within this model, and there is evidence that this has been achieved in some studies, it is imperative that the methodological complexities peculiar to homoeopathy are understood and that trial designs are predicated on this complexity.

Many attempts at adequate investigation of homoeopathy through research have been stymied by the absence of the individualised approach typical of everyday homoeopathic practice. In such studies, prescribing may be based on pathology rather than the patient’s characteristics, for example, or isopathic preparations or combinations (complexes) of homoeopathic medicines may be employed, contradicting the principles of so-called ‘classical’ (simplex) homoeopathy. Trial size, a critical factor in assessing trial validity, may be influenced by economic factors in a way that is disadvantageous to homoeopathy (Chatfield & Relton, 2005). For instance, the largest trials are likely to be those testing isopathic preparations or complex homoeopathic products. The preference for such preparations of homoeopathic medicine may be due to the fact that they are marketable as ‘over-the-counter’ products, if proven efficacious, and hence these trials are likely to attract the resources of large pharmaceutical companies.

In the conventional research model, high methodological quality is defined as high internal validity, while the requirements for external validity are ignored. External validity relates to the clinical relevance of a medical intervention and to the real world applicability of a study’s findings. In fact,
in placebo controlled randomized controlled trials, it could be said that high internal validity is gained at the expense of external validity. This relates to the distinction between efficacy and effectiveness of medical interventions (Fisher, 2008b). Efficacy can be established under restricted ‘ideal’ conditions, such as apply in a research trial, while effectiveness describes real-world conditions. The clinical effectiveness of a treatment pertains to the multiplicity of factors met in population usage, where length of use of a drug, side effects, co-morbidities and drug interactions are ultimately displayed. A drug deemed highly efficacious following clinical trials may later be withdrawn once real-world conditions of its use exhibit effects beyond the data provided by the original trial. Assessments of clinical effectiveness and responsiveness to findings at this level of evidence are clearly vital.

These considerations place RCTs in context as a valuable research tool, but not the sole deciding factor in health care delivery (Booth, 2009). In homoeopathic research, more comprehensive measures encompassing clinical effectiveness may be established through research comparisons of usual care with the new interventions, and through observational studies, which more readily capture real world conditions. Material derived from observational data and from case studies is included in hierarchies of evidence, though well down that grading of evidence, which valorizes the RCT at the expense of material describing clinical effectiveness. A holistic, real world application of ‘evidence-based medicine’ would have the capacity to integrate individual clinical expertise with the best available evidence from systematic research (Sackett et al, 1996). Returning to the more discrete focus of systematic reviews and meta-analyses, the validity of these
tools of course rests upon the quality of the randomized controlled trials selected and assessed.

4.ii. **Meta-analyses:**

It has been noted that “..the main criticism of homeopathic research is the lack of high-quality trials…” (Lin & Myers, 2005). These same authors remark however that “this criticism can also be applied to clinical trials in general” (p.359). The issue of quality of RCTs in homoeopathy has nevertheless been cited by many authors (Cucheret, 2000; Hornung & Vogler, 1990; Hornung, 1991; Mathie, 2003 amongst others) and attention has been paid to guidelines for research meeting both the conventional criteria for sound conduct of research and the specific requirements of homoeopathic research (Crpanne, 1985; Dangouman, 1996; Hornung, 1991; Haidvogl, 1994).

As noted, the validity of comprehensive reviews of homoeopathic research relies on the quality of the RCTs included in the reviews. Bearing this in mind, some of the research material can be discussed. In four out of five frequently cited meta-analyses of homoeopathic research, the researchers have reached the qualified conclusion that homoeopathy differs from placebo (Kleinjen, et al, 1991; Boisell, et al, 1996; Cucherat & Linde, 2000; Linde et al, 1997). Three of these meta-analyses can be explored in some detail to assess their validity. (In the preparation of this material, the extensive research undertaken by Dr. Stephen Myers (Lin et al, 2005) has been a useful resource. The section of the document in Lin et al (2005)
devoted to homoeopathy (see Appendix 3 of that paper) provides a useful grading of trials in homoeopathy and a detailed discussion of the topic.)

A Dutch study led by Kleijnen (Kleijnen, et al 1991) produced its review of 107 clinical trials in homoeopathy on the basis of rigorous assessment guides (Wilson & Henry, 1992). It included seven methodological criteria: the quality of the description of the patient characteristics, the number of patients analysed, the type of randomisation implemented, randomisation, the degree of clarity of description of the methods, double-blinding, effect of measurement relevant and well-discussed and the quality of the description of the results. These criteria were allocated points to a maximum of 100: twenty-one studies scored greater than 55%, eight of which scored 80% or higher. Of the 107 trials, 81 yielded positive results, two were uninterpretable while the remaining 24 showed no significant difference between homoeopathic drugs and placebo. The results of this meta-analysis were reported in the British Medical Journal (1991). The following table outlines the results of the trials cited by Kleijnen, et al, 1991:

<table>
<thead>
<tr>
<th>Diseases</th>
<th>No of trials</th>
<th>Positive results/total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>9</td>
<td>4/9</td>
</tr>
<tr>
<td>Respiratory infections</td>
<td>19</td>
<td>13/19</td>
</tr>
<tr>
<td>Other infections</td>
<td>7</td>
<td>6/7</td>
</tr>
<tr>
<td>GIT diseases</td>
<td>7</td>
<td>5/7</td>
</tr>
<tr>
<td>Post-operative ileus</td>
<td>7</td>
<td>5/7</td>
</tr>
<tr>
<td>Hay fever</td>
<td>5</td>
<td>5/5</td>
</tr>
<tr>
<td>Rheumatic disease</td>
<td>6</td>
<td>4/6</td>
</tr>
</tbody>
</table>
The mean score of the 107 trials was 42.3% (ranging from 0% to 90%). The wide variation in the trials meant that the results could not be pooled statistically, and publication bias was evident in the small number of trials published with non-significant or negative results. Despite these shortcomings in the research method of individual trials, this meta-analysis was judged to be of an overall high quality and it demonstrated evidence of the efficacy of homoeopathy. While they emphasised the need for greater rigour when designing trials in homoeopathy, and for clear descriptions of the methodology, the authors of this study concluded: “The evidence presented in this review would probably be sufficient for establishing homoeopathy as a regular treatment for certain conditions” (Kleijnen, et al, 1991, p.321).

Trial quality is assessed before a trial can be included in a meta-analysis or systematic review. In Linde et al (1997) the researchers selected inclusion criteria to improve the overall quality of their meta-analysis. They examined 89 of 186 identified trials, ensuring that those trials selected were:

i) on people being treated for an illness or entered into a prophylactic trial;
ii) placebo-controlled;
iii) randomised or double-blinded;
iv) accompanied by a written report of the trial, and
v) able to permit outcome-rate calculations to be assessed through the provision of sufficient data. Jadad criteria was used to assess the trials qualitatively (Jadad et al, 1996). Of these trials, 29% met the criteria for ‘high quality’ and this review was of a higher quality than that by Kleijnen, et al (1991). Quantitative analysis indicated an overall odds ratio of 2.45 in favour of homoeopathy (95% CI: 2.05-2.93) though this was reduced to 1.66 (95% CI: 1.33-2.08) when only the high quality studies were included. Further stringency measures such as correction for publication bias reduced the odds ratio by about 27% but statistical significance was maintained. The absence of clinical replications for any of the trials was noted, and the authors cautioned that there were few if any implications for clinical practice because “there was insufficient evidence that homoeopathy is clearly efficacious for any single clinical condition” from this analysis. The authors noted, however, that the results of the meta-analysis were “not compatible with the hypothesis that the clinical effects of homoeopathy are completely due to placebo” (Linde et al, 1997).

A further meta-analysis was conducted by Linde & Melchart (Linde & Melchart, 1998) and was restricted to trials using individualised homoeopathic prescriptions and was therefore designed to be more consistent with homoeopathy as it is practised. In this case, the expectation of researchers was that the more stringent application of homoeopathic method would be more likely to achieve positive research outcomes in this review of trials. The significant, but smaller effect established in this study (RR = 1.62 (CI 1.17-2.23)) vanished when only the higher quality trials were included – a negative, and counter-intuitive, outcome for homoeopathy.
(Linde, et al 1999). An inverse relationship between trial quality and significance has been noted however, in both homoeopathic (Linde, 1999) and conventional medical research (Moher, et al, 1998).

In a meta-analysis by Cucherat et al (Cucherat et al, 2000) all of the published and unpublished randomised controlled trials in homoeopathy were identified up to June 1998 on the basis of those which:

i) compared homoeopathic treatment with either placebo or a treatment without an active constituent;

ii) used a dilution of greater than 1 part per million; and

iii) had a clearly defined primary outcome.

The researchers used a broad-based question to test the efficacy of homoeopathic treatment in patients with any condition, creating some problems in relation to conventional statistical analyses. Significance levels (p values) were combined in order to overcome these. The null hypothesis tested then was that homoeopathic efficacy was not demonstrated in any of the included trials. The combined p value for the 17 comparisons was 0.000036, which was reduced to 0.082 when only the five highest-quality trials were included, and demonstrated an inverse relationship between trial quality and significance, as noted by Linde, et al (1999) and Moher et al (Moher, et al, 1998). While efficacy was not supported in all trials, Cucherat et al (2000) found that in at least one trial, homoeopathic treatment was more efficacious than placebo. These authors noted that: “There is some evidence that homoeopathic treatments are more effective than placebo; however the strength of this evidence is low because of the low methodological quality of the trials” (Cucherat et al, 2000).
As noted by Kleinjen (Kleinjen et al, 1991) there is no reason to believe that deficiencies in methodology are limited to homoeopathic research. Researchers in homoeopathy appear candid in acknowledging such problems and in addressing remedies for them. The scrupulous attention to research protocols detailed in the above meta-analyses provides a contrast with that in the study by Shang et al (Shang et al 2005) described below.

4.iii. The meta-analysis by Shang et al (2005)

The study by Shang et al (Shang et al, 2005) is especially relevant to the NH&MRC review due to the prominence given to this meta-analysis by the House of Commons STC Evidence Check 2: Homeopathy. The report of the U.K. homoeopathy inquiry is specified by the NH&MRC as its primary source of information in its own investigation into homoeopathy. In a letter to the AHA, dated May 25th, 2011, the NH&MRC states that:

“The NH&MRC is currently reviewing evidence to inform the development of a position statement on homeopathy based on a report from the United Kingdom House of Commons Science and Technology Committee: Evidence Check 2: Homeopathy – Fourth Report of the Session 2009-10.”

It is of considerable concern to the AHA that the NH&MRC would limit its inquiry to a single source of information, and the present document places a broader view before the NH&MRC in order to assist the Council to overcome this limitation.
In the conduct of its inquiry, the House of Commons STC received 56 submissions of written evidence yet appears to rely almost exclusively (paragraph 69 of the STC) on the evidence from the meta-analysis of Shang et al (Shang et al, 2005) in arriving at its negative findings on the efficacy of homoeopathy. Given this focus, it is important to discuss that study in some detail and canvass appraisals of the study by other researchers in the field.

The STC describes the study by Shang et al as “the most comprehensive to date”, without noting in its discussion that the study has been the subject of criticism of the type which would ordinarily moderate appraisal. Principle among this criticism was the fact that The Lancet published this work despite the failure of the meta-analysis of Shang et al to conform to that publication’s QUOROM guidelines (Moher et al, 1999) for such research (Ludtke & Rutten, 2008).

Summarising the results of the study by Shang et al, the STC declared that it “arrived at a devastatingly negative overall conclusion” (HOC STC report 2010) for homoeopathy. This summary could be viewed as an over-statement of the findings of the Shang study, which by contrast read that: “...there is no convincing evidence that homoeopathy was superior to placebo,” and that there was “weak evidence for a specific effect of homeopathic remedies” (Shang et al, 2005). These statements from Shang’s study, while far from an endorsement of homoeopathy (Baldwin, 2010) could equally be seen as neutral or as weak-positive findings, but were interpreted for the committee by Professor Edzard Ernst (HOC evidence 26, 27 & 51) into a “devastatingly negative” report on the efficacy of homoeopathy over placebo (HOC report, p. 18). Ernst’s view is endorsed by
the STC without reference to the range of alternative, scholarly and more nuanced views put before the committee (Evidence 21; 37 & 53; 130; 138 & 143; 166; 173 and others).

Both the methodology and the conclusions in the meta-analysis by Shang et al have been challenged by other researchers in this field (Chatfield & Relton, 2005; Ludtke & Rutten, 2008; Rutten & Stolper, 2005). Their concerns are that:

- in 5 of the 8 homoeopathic trials studied by the group the same homoeopathic medicine was given to every subject in the trial limiting the relevance of the study to homoeopathy-as-practised;
- more recent and larger trials which were available at the time of the research were not included;
- the inclusion of a trial for the prophylactic use of Arnica further skewed the study away from typical homoeopathic clinical practice, as did the inclusion of a trial for Thyroidinum for weight loss;
- the sub-group of selected homoeopathic trials was not matched with the conventional trials (cut-off values differed for the groups);
- the quality of the trials were not matched (the homoeopathic trials were of higher quality than that of the conventional trials
- the severity of the complaints in the homoeopathic and conventional groups were not matched
- definitions relating to ‘larger trials’ and ‘higher quality’ criteria were not provided;
- a sensitivity analysis was not included
- the impression is given that 110 trials (110 of each homoeopathic and 110 conventional) were included in the meta-analysis while in fact 8 homoeopathic and 6 conventional trials were studied;
- the researchers failed to provide information about selection criteria for the eight high quality studies chosen, and
- information regarding which trials were included was not provided

Ludtke et al (Ludtke et al, 2009) commented further on the methodological problems when post-publication data from the study eventually became available: “The heterogeneity of trials is high and the meta-analysis results are not robust against small changes in study design or statistical analysis,” calling into question the results of this group’s analysis. It is noted that of several comprehensive reviews of homoeopathy emerging from the same institute as the Shang group’s study (the Department of Social and Preventative Medicine, University of Berne), the latter is the only analysis from that institute to reach negative or equivocal findings in relation to homoeopathy. That a single study and one of such porosity as that of Shang et al (2005) should be used to declare the “death of homoeopathy” (The Lancet, 2005) simultaneously diminishes the name of science and the prestige of that journal.

To counter the transparent bias in favour of the Shang group’s study and the apparent bias against all other views put before the STC, the AHA urges the NH&MRC to review all of the material submitted to the STC. The AHA directs attention particularly to the submissions presented by Doctors Sara Eames and Peter Fisher of the British Homoeopathic Association and those from the Faculty of Homoeopathy, the European Committee for
Homoeopathic Medicine, the Liga Medicorum Homoeopathica Internationalis, the Society of Homoeopaths, the Homoeopathy Research Institute and the Complementary Medicine Research Group of the University of York. In its submission to the STC, the latter group noted that:

“To date, there are eight systematic reviews that provide evidence that the effects of homoeopathy are beyond placebo when used as a treatment for (five childhood conditions).”

This statement made by the University of York research group stands in contrast to that provided by Professor Ernst, yet fails to be acknowledged or to find its way into the assessment made by the STC in evaluating the evidence for the clinical efficacy of homoeopathy. The University of York research centre belongs to the mainstream of medical science, and was ranked joint-first in the U.K. nationally for health sciences research in the 2010 Research Assessment Exercise. As Edward Baldwin comments in his response to the outcome of the STC:

“...the committee favoured the views of two of its invited witnesses (Professor Ernst and Dr. Ben Goldacre) known for their opposition to homoeopathy,” while it “failed to adequately scrutinise the evidence of the University of York researchers - representatives of an awarded centre of excellence in research” (Baldwin, 2010, www.britishhomeopathic.org).

The four meta-analyses discussed earlier in this paper stand in contrast to that of Shang et al, both in their measured outcomes and in the quality of the tools by which these outcomes were reached. The singular focus of the STC on one review of highly questionable quality is to be deplored and must be
challenged. In support of this challenge, the AHA takes the opportunity of
documenting for the NH&MRC an overview of research in homoeopathy.
The homoeopathic researches undertaken by Dr. Robert Mathie (Mathie,
2010), who scrutinised homoeopathic to identify the best quality trials and
reviews of trials, provides the source of the material presented here for the
attention of the NH&MRC.

4.iv. **Overview of homoeopathic research: the work of Dr. Robert Mathie.**

A summary of the “*best clinical research evidence in homeopathy published*
*in peer-reviewed scientific journals up to and including October 2009*” was
compiled by Dr. Robert Mathie and presented to the House of Commons
STC. This considered and careful work by the research development officer
of the British Homoeopathic Association was apparently disregarded by the
STC in their deliberations on homoeopathy. Reviewer bias is a phenomenon
observed not infrequently in relation to unconventional therapies (Resch et
al, 2000), and is not necessarily responsive to the quality of the work
reviewed.

Mathie’s overview canvassed the meta-analyses already addressed above, as
well as systematic reviews of

a. research focusing on particular medical conditions
b. research focusing on particular groups of diagnoses.

Mathie then provided a
c. comprehensive overview of all randomised clinical trials conducted in
homoeopathy from 1950 till 2009.
d. a review of randomised, non-controlled trials and of non-randomised, non-controlled trials in homoeopathy.

a. Seventeen reviews studied by Dr. Mathie focussed on particular medical conditions, avoiding the heterogeneity of medical conditions. Five reviews concluded there was a positive effect for homoeopathy:
   - post-operative ileus (Barnes, et al, 1997)
   - seasonal allergic rhinitis (Wiesenauer, & Ludtke, 1996; Taylor et al, 2000) and

Three reviews concluded there was little or no evidence of an effect from treatment in the following three conditions: attention-deficit hyperactivity disorder (Coulter & Dean, 2007), delayed-onset muscle soreness (Ernst & Barnes, 1998) and headache and migraine prevention (Ernst, 1999). In nine systematic reviews, a clear conclusion regarding response to treatment could not be reached. These were trials in anxiety (Pilkington, et al, 2006), chronic asthma (McCarney, et al, 2004), dementia (McCarney, et al, 2004), depression (Pilkington, et al, 2005), headache and migraine treatment (Owen & Green, 2004), HIV/AIDS (Ullman 2003), induction of labour (Smith, 2004), influenza (Vickers & Smith, 2006) and osteoarthritis (Long & Ernst, 2001).

b. Seven systematic reviews focused on particular groups of diseases. Of these, four were found to be positive:
   - allergies (Bellavite et al, 2006)

Two reviews were negative: ailments of childhood and adolescence (Altunc, et al, 2007) and the review of trials of the homoeopathic treatment of cancer (Milazzo et al 2006); one review of treatment for the side-effects of cancer (Kassab et al, 2009) was non-conclusive.

Arnica, well known in homoeopathy for bruising and soreness from injury or over-use, has been the subject of a number of trials. The two reviews of Arnica studies canvassed by Mathie derived negative results (Ernst & Barnes 1998; Ernst & Pittler, 1998). (These Arnica trials demonstrate some of the difficulties of applying homoeopathic approaches to research, and are instanced here to exemplify these difficulties. Arnica 30 was tested for efficacy in stroke using a double-blind protocol (Savage & Roe, 1977, 1978; scores 55/100 and 53/100 respectively), but no significant benefit of treatment was found. Subsequent analysis of the data however (Scofield, 1984) showed that of the 40 patients entered into the trial, only 3 had symptoms typical of the Arnica symptom picture, and that these three had showed good response to the treatment. In the 1978 trial, only one patient had Arnica symptoms, and that one was assigned to the placebo group. The results of studies using Arnica as a prophylactic for muscle soreness in marathon runners were mixed, and it has been noted that this is an unusual clinical use for this medicine. Two studies in Oslo were inconclusive (Tveiten, et al, 1998) and a London study showed no response to prophylactic Arnica (Vickers, et al, 1998). A comprehensive review of 40
studies found that 35% of these reported a significant result while ten more showed a tendency to significance (Ludtke & Wilkens, 1999), but divergent study designs in these reviews provided no common quantitative measure and so rendered the results problematic. These examples demonstrate the twin issues of individualisation in homoeopathic research and the validity problems deriving from unmatched studies.)

c. An overview of randomised controlled trials in homoeopathy.

Mathie identified 142 RCTs which met criteria for inclusion in his overview. This criteria:
- included only those RCTs published in peer reviewed journals (any country, any language) from 1950 – 2009
- applied a minimum standard of intrinsic quality, including prospective random assignment to treatment; explicit mention of double-blinding in placebo-controlled trials. In other-than-placebo trials, observer blinding was sufficient for inclusion.

Methods of data extraction applied:
* Less than half of the eligible RCT’s included a power calculation and so lacked the associated pre-defined minimum effect needed to confer clinical importance. Positive or negative findings in these studies were described only in terms of statistical significance, not clinical importance.

* A study reporting statistically significant findings was either ‘positive’ or ‘negative’ depending on whether the homoeopathy group was superior or inferior to control in at least one principal outcome. A statistically
conclusive trial result required that the 95% confidence interval (CI) of the mean difference in the outcome variable did not include 0 (or P<0.05); a statistically non-significant trial result meant that the 95% CI included 0 (or P>0.05). Other-than-placebo trials adopted relevant corresponding criteria.

* To be regarded as statistically conclusive, Mathie required at least one significant finding out of no more than three statistical analyses of a given study's principal outcomes. Secondary outcomes were disregarded. This approach avoided the possibility of interpreting a trial as statistically conclusive based on merely one statistically significant positive or negative result out of many.

The findings from RCT’s:
- 120 out of 142 trials were placebo controlled (85%)
- Other-than-placebo conditions applied to the remaining 22 RCT’s (15%)

‘Nature of the control group’ findings:
- positive in 44% of trials,
- negative in 8% and
- non-conclusive in 48%
- findings in the other-than-placebo controlled RCTs were more conclusively positive or negative more frequently than those in the placebo controlled group.

‘Mode of homoeopathy’ findings:
- 40 trials (28%) were of individualized homoeopathic treatment
- 102 (72%) of the remaining trials were for ‘standardised’ homoeopathy
- Individualised treatment was positive in 45% of cases and negative in 8%
- Standardised treatment was positive in 44% of cases and negative in 8%
- There was little difference therefore between the mode of treatment in regard to outcomes.

Research was replicated in 28 conditions out of the 80 conditions represented in this review of RCTs in homoeopathy. Single studies applied in the 52 other medical conditions.

In the review of evidence for the replicated trials, evidence is positive for:
  * Fibromyalgia (Fisher, 1986; Bell et al, 2004; Relton, et al, 2009) and
  * Sinusitis (Weiser & Clasen, 1994; Friese & Zabalotnyi, 2007; Zabalotnyi, et al, 2007);

Evidence was inconclusive for:

Insect bites (Hill et al, 1995; Hill et al, 1996)
Menopause in breast cancer (Jacobs et al, 2005; Thompson et al, 2005)
Post-operative pain or swelling (Robertson et al, 2007; Brinkaus et al, 2006; Kaziro, 1884; Lokken et al, 1995; Hart et al, 1997; Wolf et al, 2003; Stevinson et al, 2003;)

There was no identifiable balance of evidence for:

Dermatitis (Fisher, et al, 2006),
Irritable bowel syndrome (Rahlfs & Mossinger, 1976)
Leg ulcers (Garrett, et al, 1997)
Otitis media (Harrison et al, 1999; Jacobs, et al, 2001) or for

d. Mathie also reviewed non-randomised research in controlled trials and
in non-controlled trials. Non-randomised, controlled, parallel group design
models have focussed on homoeopathy for a particular condition: eczema
(Keil et al 2008), insomnia (Waldschutz & Klein, 2008), otitis media (Friese
et al, 1997), and vertigo (Klopp et al, 2005). Although results have been
positive in these studies, the absence of group randomisation prevents the

Mathie (2010) notes that non controlled, non randomised research provides
useful adjunctive data in CAM therapies (Walach, Jonas & Lewith, 2002;
White & Ernst, 2001). In homoeopathy, such findings have been strongly
positive for dysmennorrhoea (Witt et al, 2009), hot flushes (Bordet, et al,
2008), sinusitis (Witt et al, 2009) and headache (Mascari-Tomaioli et al,
2009).

Dr. Mathie’s research has been chosen for presentation here due to his
rigorous criteria in the selection of research from RCT’s (a – c above) and
the discrete groupings of his reviews which optimise matching and validity.
Mathie’s overview of research up until 2009 therefore provides a reliable
assessment of that data. What is shown within this strenuous analysis of
homoeopathic research is that homoeopathy, in certain conditions at least,
has an effect greater than placebo. These conditions include: childhood
diarrhoea, post-operative ileus, seasonal allergic rhinitis, vertigo, allergies, upper respiratory tract infections, rheumatic disease, fibromyalgia and sinusitis. Positive findings were also found in favour of an effect beyond placebo in the four meta-analyses described in detail earlier in this paper.

The placebo argument against an effect for homoeopathy is considered well challenged by the evidence presented here, as is the ‘implausability’ claim regarding ultra-dilutions in homoeopathy. The placebo responses is an acknowledged therapeutic phenomena known to occur in all therapeutic fields: the subject itself is not canvassed here because the homoeopathic research presented puts it out of consideration as an explanation for the action of homoeopathic medicines. Claims that homoeopathic responses are placebo responses act as a distraction from engagement with the challenge and the opportunity which homoeopathy presents to science and to medicine.

Homoeopathic clinicians reading Mathie’s findings (Mathie, 2009) will note the range of conditions which fall outside the discrete filters of Mathie’s evidence net. These conditions include many of which are commonly and successfully treated in homoeopathic practice (e.g. anxiety, otitis media, dermatitis, irritable bowel syndrome, post operative pain and swelling, leg ulcers, warts and insect bites, amongst many others). The narrow eye of the RCT needle has provided evidence of the effect of homoeopathic medicine beyond placebo in Mathie’s studies in the conditions specified above: the positive action of a homoeopathic potency is therefore confirmed. The broader picture of homoeopathy-as-practiced is accessible through observational studies. This perspective, in which homoeopathy is often treating chronic conditions and complex co-morbidities, provides the larger
pieces of the research puzzle: hence a more comprehensive, living picture of homoeopathy and its therapeutic capacities.

v. **Observational studies.**

Observational studies are widely used in the U.K. National Health Service in general where ‘PROMs’ or ‘patient reported outcomes measurement’ (www.dh.gov.uk) surveys are regarded as a useful tool of research. In homoeopathy, observational studies provide compelling data of the benefits of homoeopathic treatment. In the U.K., four hospitals offer out patient homoeopathic clinics (Bristol, Liverpool, Glasgow and London). At each hospital, positive outcomes have been reported in approximately 70% of patients (Sharples, et al, 2003; Spence et al, 2005; Clover, 2000, Richardson, 2001).

Mathie (Mathie 2010) reports on a survey of patient outcomes across all of the homoeopathic hospitals in the U.K. (Thompson, et al, 2008). In this study, 1602 patients with multiple complex morbidities were followed up over a one month period. Eczema, chronic fatigue syndrome, menopausal disorder, osteoarthritis and depression were the most commonly referred conditions. In total, the study identified 235 separate medical complaints treated at the hospitals during one month. At the second homoeopathic appointment, 34% of follow-up patients reported an improvement that affected their daily living. For patients at their sixth appointment, the corresponding improvement rate was 59%.
Other sites of observational studies show consistent results in improvements not only the presenting symptoms but also the overall wellbeing of the patient and a reduction in the use of conventional medicine (Spence et al, 2005). In the study by Spence et al (2005) at Bristol Homoeopathic Hospital, 6,544 patients were tracked through consecutive follow-up appointments over 6 years (= 23,473 consultations). The 7 point Likert scale was used as the outcome measure and at the end of each consultation, the patient’s responses were compared to a base line assessment. A total of 6,544 consecutive follow-up patients were given outcome scores:

70.7% (4627) reported improvement, and of these -

50.7% (3318) reported better (+2) or much better (+3).

The conclusions from the Bristol study were that homoeopathy is associated with positive health changes to a substantial proportion of a large cohort of patients with a wide range of chronic diseases. The diagnostic groups included in this study were: dermatology (19%), psychiatry (9%), rheumatology (10%), gastrointestinal complaints (9%) respiratory illness (6%), ENT (6%), neurology (includes chronic fatigue): (8%), cardiovascular disease (2%) genitourinary complaints (2%), oncology (7%), and ‘other’ (16%).

In his report to the HOC STC (HO 29), Dr. Hugh Nielson notes that the main weakness of the above study was the crudeness of the outcome measure: the strength of the work was in its size and comprehensiveness (www.publications.parliament.uk/pa/cm200910/cmselect/cmsctech/45/45w). The best treatment responses reported in the study were in childhood eczema or asthma, in inflammatory bowel disease, irritable bowel syndrome, menopausal symptoms and migraine.
Nielson canvassed other observational studies in homoeopathy for the STC. In a 500-patient survey at the Royal London Homeopathic Hospital it was demonstrated that many patients were able to reduce or stop conventional medication following homoeopathic treatment (Sharples, van Haselen & Fisher, 2003). The size of the effect varied between diagnoses: for skin complaints, for example, 72% of patients reported being able to stop or reduce their conventional medication. The study recorded that very often patients seek homoeopathy because of their concerns about the safety of conventional treatment.

The Liverpool department of homoeopathic medicine conducted an outcome survey over a 12 month period in 1999-2000 (Richardson, 2001). This survey canvassed the treatment responses in 1,100 patients: 76.6% reported an improvement in their condition since starting homoeopathic treatment and 60.3% regarded their improvement as major. 814 patients were taking conventional treatment for their condition and 424 (52%) of these were able to reduce or stop conventional medication. The main conditions treated were osteoarthritis, eczema, chronic fatigue syndrome, asthma, anxiety, headaches, inflammatory arthritis and irritable bowel syndrome.

In a prospective, multi-centre cohort study (Witt et al, 2005) with 103 British primary care practices treating 3981 patients, disease severity decreased significantly (p<0.001) over a 2 year period. Major improvements were observed for quality of life for adults and young children. 28% (1130) of the patients were children and 97% of all diagnoses were of chronic conditions with an average duration of 8.8 years. The most frequent diagnoses were allergic rhinitis in men, headache in women, and atopic
dermatitis in children.

Studies at other British and European outpatient clinics and hospitals (Andersen et al, 1999; Attena et al, 2000; Christie & Ward, 1996; Dempster, 1997; Guthlin et al, 2004; Sevar, 2000; Steinsbekk, 2005) reflect a similar pattern of strong positive response to homoeopathic treatment, frequently in chronic health conditions.

Such patient outcome studies offer a rich insight into the real world experience of homoeopathic practice. Practitioners in the more common homoeopathic workplace, the individual clinic of private practice, also seek to assess their practice outcomes, with tools for practice ‘audits’ being canvassed at conferences (Levy, 2008) and individual practitioners beginning to use measurement tools on a patient-by-patient basis. One such tool is the ‘Measure Your Own Medical Outcomes Program’ or ‘MYMOP’ which begins to generate a body of publications on the use of this measure (sites.pcmd.ac.uk/mymop/) of individual practice workplaces.

vi. Directions for research in homoeopathy

The complexity of case analysis and the individualisation of treatment of homoeopathic practice demands specialised tools for an adequate research measure of this unique health intervention to be provided. All of the available research evidence emphasises the need for much more and better directed research in homoeopathy (Lin et al, 2005; Ludtke, 2009; Mathie, 2003, 2010; Walach, 2002). Mathie makes these recommendations for future research in homoeopathy:
“A fresh agenda of inquiry should go beyond (but include) the placebo-controlled trial. Each study should adopt research methods and outcomes measurements linked to questions addressing the clinical significance of homoeopathy’s effects” (p.84).

The challenge for research in homoeopathy is the development of suitable trial design and tools of measurement adequately reflecting the ‘whole person’ practice central to homoeopathy (Walach, 1998; 2006). The individualised prescription applies in homoeopathic practice, whatever the medical condition being treated. The absence of individualising in research has been a significant barrier to homoeopathic research which must be overcome in future protocols. An early clinical trial for rheumatoid arthritis (Gibson et al, 1980) provided a model for homoeopathic research sympathetic to homoeopathic individualisation, which has been employed by other researchers. In this model, the standard homoeopathic examination is undertaken for all trial participants, the optimal drug selected for each subject (individualisation), and randomisation carried out after this point, with one group receiving the treatment and one receiving placebo.

Other researchers (Lin et al 2005) go further and challenge the usual parameters of scientific research by positing that single-subject research, where the subject acts as their own control, may be particularly suited to the needs of homoeopathic research. The ‘n-of-one’ trial allows the practitioner to select the optimal treatment for the subject and provides a model suitable to clinical practice. Multiple single-subject trials can then be pooled, enabling a level of external validity (Johannessen, Fosstvedt & Petersen, 1991). The requirement for a homogenous sample is thus avoided and the
conditions for a valid homoeopathic form of whole-person practice is provided through this research structure.

Measures which focus solely on physical determinants of health may be especially unsuitable to homoeopathic treatment of chronic disease states, where quality of life measures may provide more appropriate tools (Mathie, 2003; Walach, 2002). Trials of homoeopathic treatment of acute conditions may be more suited to the placebo controlled trial model, as in acute disease there is a smaller range of more commonly used medicines and the short time-frame of response to treatment in these cases provide a suitable focus for RCTs.

Mathie (2003) also proposes that equivalence trials would offer promising directions for research design. In these, a conclusion of ‘similar clinical outcome’ between homoeopathic and orthodox treatments would be based on an ability to accept statistically equivalent confidence levels in the two groups of data. Mathie suggests this technique is preferable to assuming equivalence based merely on the failure to reject the null hypothesis in a typical superiority trial (Mathie, 2003). Formal equivalence trials would also enable the further examination of the relative safety and cost-effectiveness of homoeopathy compared with conventional medicine, a potentially rich seam of useful data given both the low toxicity and the low production costs of homoeopathic medicines.

Research protocols have most typically compared homoeopathic treatment with placebo: presumably originating in the supposition that homoeopathic medicines are placebos. Such a research question may not be the most
ideal for homoeopathic investigations. More useful for homoeopathic research may be a comparative model, comparing homoeopathy with other treatments. The narrow focus of conventional drug trials are especially limiting in homoeopathic research as is the limited time frame of typical trials. Response to medications for chronic conditions in homoeopathy may include an initial period of aggravation of symptoms, for example, an adequate research measure would need to take this into account. Homoeopathic effects typically elicit ‘wellbeing’ responses, better measured with quality of life assessment tools rather than typical symptom scores, as noted earlier. A wider frame of research reference would extend to comparisons of the relative cost of homoeopathic and non-homoeopathic treatments so that decisions regarding medical interventions may take this critically important aspect of health care into account.

To further the very valuable contribution which homoeopathy may make to community health care, the scope and quality of homoeopathic research must be enhanced: this project requires greater collaboration between homoeopathic practitioners, conventional physicians and scientists.

5. Discussion

Clinical research in homoeopathy represents a meeting point of two distinct paradigms and must necessarily meet the requirements of both. Many challenges present themselves in this regard. One relates to technical
matters of research methodology and to the grading given to various research tools. Greater challenges however may come in less tangible but perhaps more powerful forms – attitudinal, philosophical and political stances may stymie communication in a way that is detrimental to the interests of the community in regard to health care information, health care choice and access to services.

Australians have embraced CAM options in health care and these choices are mirrored in congruent life-style changes, enhancing the quality of life and contributing to the prevention of disease. Most patients of CAM practitioners perceive their choice to be that of complementary health care, and most remain in regular contact with conventional service providers, and access conventional treatment where this is required. In her opening address to the WHO congress on traditional medicine in 2008, the Director-General of the WHO Dr. Margaret Chan said:

"The two systems of traditional and Western medicine need not clash. Within the context of primary health care, they can blend together in a beneficial harmony, using the best features of each system, and compensating for certain weaknesses in each. This is not something that will happen all by itself. Deliberate policy decisions have to be made. But it can be done successfully."

Immediately prior to the submission of this document, it was learned that the NICM bid for funding to establish a Cooperative Research Centre in Complementary Medicine has not been successful. That this flagship body should falter in its efforts to promote sound research into integrative health
care in Australia is highly regrettable. Such a decision suggests that public policy chooses a direction opposite to that in which the community is moving.

An ethical health care system would research the benefits, safety and costs of various models of health care interventions, provide this information to the community and facilitate access to choice in health care to all in the community. This paper presents evidence of the efficacy and clinical effectiveness of homoeopathic medicine, and benefits in relation to cost and safety are found in homoeopathic research: these characteristics suggest that an ethical direction in health care would include a commitment of resources to further research in this area of medicine.

The AHA relies upon the NH&MRC to take a more comprehensive, fair and just approach to matters of the appraisal of research, to health care policy and to patient and practitioner autonomy than that adopted by the House of Commons in its Evidence Check 2: Homeopathy. The AHA would be pleased to offer any further assistance to the NH&MRC and commends this brief exposition on homoeopathic medicine research to the Council.
References


British Homoeopathic Association:
[www.britishhomeopathic.org/research/science_and_technology_committee_report.html](http://www.britishhomeopathic.org/research/science_and_technology_committee_report.html)


*Homoeopathic Research Institute*: principals: Dr Alexander Tournier PhD., Clare Relton MSc., Dr Robert Mathie PhD., Dr Elizabeth Thompson BAOxon MBBS MRCP FFHom., Prof. Kate Thomas, Dr Lionel Milgrom PhD., Dr Mike Emmans Dean Ph.D., Dr Nagin Lad PhD., Dr Natasha Peric-Concha PhD., Dr Patti Bayliss MB., ChB FRCGP www.homeoinst.org/document-archive


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herbal medicine. School of Public Health: Latrobe University.


[www.publications.parliament.uk/pa/cmselect.cmsctech/45/09112511.htm](http://www.publications.parliament.uk/pa/cmselect/cmsctech/45/09112511.htm)


Thompson, E. A., Mathie, R T, Baitson, E S, Barron, S J, Berkovitz, S R,


Vonsyhomeopathy.wordpress.com/2010/02/27/stop-funding-nhs-homeopathy-mps-urgwho-are-these-mps/#more-293.


(10e8) and the effect of homoeopathically prepared thryoxine (10-30) on highland frogs-a multi-researcher study. Res Compl Med/Forsch Komplementared, 14:353-357.


**Attachment 1**
INTRODUCTION TO THE AHA (Australian Homoeopathic Association Inc.)

Origins and Objectives of the AHA

The origins of the Australian Homoeopathic Association date from 1946, with the Australian Institute of Homoeopathy. The Australian Homoeopathic Association Inc (AHA) was formed in 1995 from the merger of the New South Wales, South Australia and the Victoria/Tasmania branches of the Australian Federation of Homœopaths, the Australian Society of Homœopaths (Queensland), and the Oceanic Homœopathic Research Foundation (Western Australia). In 1997, further mergers were agreed with the Homœopathic Association of New South Wales, and the Australian Federation of Homœopaths in Queensland and Western Australia.

The AHA is the only national homœopathic association representing professionals in Australia, with branches in six states. The objectives of the AHA include:

- Advance the study and practice of homœopathy.
- Provide a code of professional conduct and ethics for homœopaths.
- Provide continuing professional development for homœopaths.
- Protect and promote the interests of homœopaths.
- Raise the public profile of homœopathy.
- Promote unity within the profession.
- Develop national and international links with other homœopaths and homœopathic organisations.

Structure

The AHA is run by elected Professional members. State Committees are elected annually by the Professional members of that State. National Council is the governing body and consists of one representative from each State Committee, plus three members elected by national ballot. National Council meets twice a year at a rotating venue, with other day to-day business being conducted with the assistance of the AHA National Administrator via mail, email, telephone and teleconferences as required.

Attachment 2
INTRODUCTION TO AROH (Australian Register of Homœopaths)

Origins and Objectives of AROH
The Australian Register of Homœopaths (AROH) was established in 1999 by the homœopathic profession. Its objects are as follows:

- Developing and operating a Register of Practitioners and, without limiting the generality of the foregoing, to record information relating to individual qualifications and competencies;
- Promoting, enforcing and assisting the development of industry standards for homœopaths practising in Australia;
- Issuing practising certificates and developing, conducting and promoting systems for the accreditation and/or certification of practising homœopaths in Australia based upon individual qualifications and competencies;
- Providing public interest information from its records;
- Developing, promoting and administering the standard of professional practice for practising homœopaths in Australia;
- Developing, operating and enforcing through its membership, systems to determine, resolve and prevent complaints against practising homœopaths in Australia by their clients or other practising homœopaths;
- Encouraging and promoting the activities of the Company and doing all things necessary for and incidental to the advancement of these objects.

AROH is a non-profit company limited by guarantee. Its essential mission is to protect the public from incompetent or unethical homœopathic practice. To ensure that it carries out this mission, not less than 30% of directors must be independent directors, drawn from legal, accounting, training, education, consumer protection, government or other relevant backgrounds.

Registration of Practitioners by AROH

The criteria of competency used by AROH for the registration of practitioners are the National Competency Standards for Homœopathy, which are incorporated within the National Health Training Package (NHTP). From 1 January 2003 practitioners seeking registration with AROH must either enrol in approved courses offered by Registered Training Organisations (RTOs) which conform to the NHTP, or be assessed for recognition of prior learning. Applicants who have successfully completed courses conforming to this standard may be admitted to registration provided that they:

- hold a Senior First Aid Certificate
- hold professional indemnity insurance.

To maintain their registration, practitioners must also comply with AROH’s Policy on Continuing Professional Development (CPD).
**Professional Conduct**

AROH has adopted a Code of Professional Conduct and a set of Standards of Practice. All registered practitioners are expected to abide by these, and will be held to account for their professional conduct and standard of practice. AROH has also adopted a set of Procedures for the Investigation of Professional Conduct and Standards of Practice. These are based on the procedures contained in the Traditional Chinese Medicine Act of Victoria, adapted for use by a private, non-statutory organization.
Appendix 2
**Summary of Reviewed Studies**

**Randomised Controlled Trials of Homoeopathy**

In the following tables, studies older than 10 years have been highlighted.

### 2.1. Human RCTs in conditions with a clearly positive direction of evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Condition</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frei et al. (2005)</td>
<td>ADHD</td>
<td>At entry to the crossover trial, cognitive performance such as visual global perception, impulsivity and divided attention, had improved significantly under open label treatment (P &lt;0.0001). During the crossover trial, the parent ratings were significantly lower under verum (average 1.67 points) than under placebo (P =0.0479). Long-term improvement reached 12 points (63%, P &lt;0.0001).</td>
</tr>
<tr>
<td>Jacobs et al. (2005b)</td>
<td>ADHD</td>
<td>43 children in a partial cross-over double-blinded alternate placebo controlled study. Scores for initial verum subjects were compared with placebo, and those placebo scores were compared with the same subjects after they later took verum. Significant differences were found for both comparisons.</td>
</tr>
<tr>
<td>Bell et al. (2004)</td>
<td>Fibromyalgia</td>
<td>53 patients showed significant improvement in response to individualised prescribing with tender point count and tenderness reduced (p=0.008), and questionnaire at 4mths indicated the verum was more helpful 0.004</td>
</tr>
<tr>
<td>Fisher (1986)</td>
<td>Fibromyalgia</td>
<td>Using Arnica, Bryonia and Rhus tox vs placebo, prescribed individually on their symptoms, homeopathy produced a significant improvement, but only when the prescribed remedy was well indicated.</td>
</tr>
<tr>
<td>Fisher et al. (1989)</td>
<td>Fibromyalgia</td>
<td>30 patients with characteristics indicating Rhus tox were given this remedy or placebo in a double-blind crossover trial. The number of tender spots was reduced in the verum (p=0.005).</td>
</tr>
<tr>
<td>Relton et al. (2009)</td>
<td>Fibromyalgia</td>
<td>47 patients were randomised, 20 completed individualised Hom Rx, whose symptoms were significantly improved at 22 weeks as determined by questionnaire.</td>
</tr>
<tr>
<td>Belon et al. (2006)</td>
<td>Heavy metal toxicity</td>
<td>The administration of “verum” appeared to make positive modulations of several parameters. Most of the subjects reported better appetite and improvement in general health, thereby indicating possibility of its use in remote arsenic-contaminated areas as an interim health support measure to a large population at risk.</td>
</tr>
<tr>
<td>Belon et al. (2007)</td>
<td>Heavy metal toxicity</td>
<td>52 patients suffering from mercury intoxication were randomly assigned to receive the homeopathically prepared mercury (Merc sol) or a placebo. Quality of life assessments and mercury in blood, urine and hair tests were made a priori, at 30 and 60 days. It was found that the verum significantly decreased mercury in hair, with indication of increase in urinary elimination and improvement in symptomatology.</td>
</tr>
<tr>
<td>Beringhs-Bueno et al. (2006)</td>
<td>Heavy metal toxicity</td>
<td>52 patients suffering from mercury intoxication were randomly assigned to receive the homeopathically prepared mercury (Merc sol) or a placebo. Quality of life assessments and mercury in blood, urine and hair tests were made a priori, at 30 and 60 days. It was found that the verum significantly decreased mercury in hair, with indication of increase in urinary elimination and improvement in symptomatology.</td>
</tr>
<tr>
<td>Padilha et al. (2011)</td>
<td>Heavy metal toxicity</td>
<td>52 patients suffering from mercury intoxication were randomly assigned to receive the homeopathically prepared mercury (Merc sol) or a placebo. Quality of life assessments and mercury in blood, urine and hair tests were made a priori, at 30 and 60 days. It was found that the verum significantly decreased mercury in hair, with indication of increase in urinary elimination and improvement in symptomatology.</td>
</tr>
<tr>
<td>Study</td>
<td>Condition</td>
<td>Outcomes</td>
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<td>-------------------------------</td>
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</tr>
<tr>
<td>Brydak and Denys (1999)</td>
<td>Influenza</td>
<td>The administration of Gripp-Heel significantly raised haemagglutinin and neuraminidaseA1, N2 and NB levels compared to placebo.</td>
</tr>
<tr>
<td>Ferley et al. (1989)</td>
<td>Influenza</td>
<td>578 patients randomly assigned to Oscillococcinum or placebo during 1987 H1N1 epidemic. Recovery in 48hrs was significantly greater in the verum p=0.03.</td>
</tr>
<tr>
<td>Papp et al. (1998)</td>
<td>Influenza</td>
<td>372 patients. After 48 hours the symptoms of the patients in the verum group were significantly milder (P&lt;0.023) than in the placebo group. The number of patients with no symptoms was significantly higher in the verum group from the second day onwards (verum: 17.4%, placebo: 6.6%) until the end of the patients' recording (day 5 in the evening: verum: 73.7%, placebo: 67.7%). The biggest group difference was recorded for the time between the evening of the second day (10.6% more patients with no symptoms) and the morning of the fourth day (10.2% more patients with no symptoms).</td>
</tr>
<tr>
<td>Bell et al. (2011)</td>
<td>Insomnia</td>
<td>Verum remedies significantly increased PSG total sleep time and NREM, as well as awakenings and stage changes.</td>
</tr>
<tr>
<td>Brooks et al. (2010)</td>
<td>Insomnia</td>
<td>Different Responses were observed to Coffee 30 and Nux vomica 30 as compared to placebo in this group of patients who a priori exhibited symptoms indicative for the use of these remedies.</td>
</tr>
<tr>
<td>Carlini et al. (1987)</td>
<td>Insomnia</td>
<td>This study provides preliminary evidence for beneficial effects of Dysto-loges S on sleep quality</td>
</tr>
<tr>
<td>Hellhammer and Schubert (2012)</td>
<td>Insomnia</td>
<td>The individually prescribed homeopathic remedies were associated with a significant increase in sleep duration compared to the placebo patients.</td>
</tr>
<tr>
<td>Naude et al. (2010)</td>
<td>Insomnia</td>
<td>121 patients demonstrated over 10 weeks that Zeel comp tds was slower to reduce symptoms than 25mg Diclofenac daily, its effectiveness was approaching that of Diclofenac by the end.</td>
</tr>
<tr>
<td>Maronna (2000)</td>
<td>Osteoarthritis</td>
<td>Zeel Comp was of equivalent efficacy, less expensive and mildly better tolerated.</td>
</tr>
<tr>
<td>Nahler et al. (1998)</td>
<td>Osteoarthritis</td>
<td>A double-blinded study of 65 patients found better pain relief in the homeopathic group (55% achieved measured relief from homeopathy as compared to 38% from acetaminophen) which did not reach statistical significance. Many of the patients asked to continue with the homeopathic treatment</td>
</tr>
<tr>
<td>Shealy et al. (1998)</td>
<td>Osteoarthritis</td>
<td>114 patients with mild to mod OA were randomised and treated double blind with either Zeel Comp or Diclofenac. In both treatment groups, significant and clinically relevant improvements in mobility and functionality of the affected knee joint were noted over the ten weeks of treatment. In addition, patients achieved greater independence and thus also greater self-sufficiency. The Diclofenac group improved more rapidly, but the Zeel Comp group were catching up by 10weeks.</td>
</tr>
<tr>
<td>van Haselen and Fisher (2000)</td>
<td>Osteoarthritis</td>
<td>The pain reduction was 16.5mm VAS in the homeopathy group (n=86) and 8.1mm in the piroxicam group (n=86); the difference between treatment groups was 8.4mm (95% confidence interval 0.8-15.9), and after adjustment for pain at baseline it was 6.8mm (95% confidence interval -0.3 to 13.8). Adverse events occurred in 28 patients (12 homeopathy group, 5 withdrawn; 16 piroxicam group, 9 withdrawn); 18 of the events involved a local reaction (7 homeopathy group, 2 withdrawn; 11 piroxicam group, 5 withdrawn).</td>
</tr>
<tr>
<td>Harrison et al. (1999)</td>
<td>Otitis media</td>
<td>At 12 mths, 64% of children receiving homeopathic care had a hearing loss less then 20 dB vs 56% standard care. More homeopathy patients than controls had a normal tympanogram (75 vs 31%, P = 0.015). Referrals to specialists and antibiotic consumption was lower in the homeopathy group, though differences between groups did not reach statistical significance.</td>
</tr>
<tr>
<td>Jacobs et al. (2001)</td>
<td>Otitis media</td>
<td>Significant decrease in symptoms at 24 and 64 hrs after verum treatment p&lt;0.05.</td>
</tr>
<tr>
<td>Study</td>
<td>Condition</td>
<td>Outcomes</td>
</tr>
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</tr>
<tr>
<td>Taylor and Jacobs (2011)</td>
<td>Otitis media</td>
<td>A total of 119 eligible children were enrolled in the study; symptom diaries were received from 94 (79%). Symptom scores tended to be lower in the group of children receiving ear drops than in those receiving standard therapy alone; these differences were significant at the second and third assessments (P = 0.04 and P = 0.003, respectively). In addition, the rate of symptom improvement was faster in children in the ear drop group compared with children in standard therapy alone group (P = 0.002).</td>
</tr>
<tr>
<td>Sinha et al. (2012)</td>
<td>Otitis media</td>
<td>Individualized homeopathy is as effective as conventional treatment in AOM, but symptomatic improvement was quicker in the Homeopathy group, and there was a large difference in antibiotic requirements, favouring homeopathy.</td>
</tr>
<tr>
<td>Aabel (2000)</td>
<td>Seasonal allergic rhinitis</td>
<td>No statistically significant difference between the groups was found during the first and last period of May. However, from 8 to 18 May, a clinically interesting difference was revealed between the groups, those receiving Betula 30c having fewer and less serious symptoms. For some days these differences were statistically significant. Surprisingly, this group reported more aggravation from the tablets than did the placebo group.</td>
</tr>
<tr>
<td>Kim et al. (2005)</td>
<td>Seasonal allergic rhinitis</td>
<td>Mixed grass pollen 30C significantly reduced symptoms and need for antihistamines in this trial with 144 patients (p=0.02). There was also significantly more initial aggravation on verum (p=0.05).</td>
</tr>
<tr>
<td>Reilly et al. (1986)</td>
<td>Seasonal allergic rhinitis</td>
<td>Luffa comp.-Heel ™ Nasal Spray consisted of a fixed combination of Luffa operculata, Galphimia glauca, histamine, and sulfur. The 146 patients demonstrated over 6wks, therapeutic equivalence between the two forms of treatment.</td>
</tr>
<tr>
<td>Wiesenauer et al. (1983)</td>
<td>Seasonal allergic rhinitis</td>
<td>Reduction of symptoms in eyes and nose was significantly greater with verum than placebo.</td>
</tr>
<tr>
<td>Wiesenauer and Ladetke (1995)</td>
<td>Seasonal allergic rhinitis</td>
<td>A randomized, double-blind multicenter RCT verifying the effectiveness of the Galphimia glauca D4 therapy. The average time of observation was 51/2 weeks. Verum was more effective than placebo at a 1% level of significance. Therapeutic success was given in 34/41 (= 83%) of the patients with Galphimia and in 21/45 (= 47%) of the control patients.</td>
</tr>
<tr>
<td>Wiesenauer et al. (1990)</td>
<td>Seasonal allergic rhinitis</td>
<td>144 patients randomised. In the homeopathic treatment group, the average sum score dropped from initially 12.1+/−1.6 to 5.9+/−2.0 points after 7 days. In the placebo group it decreased from 11.7+/−1.6 to 11.0+/−2.9 points (p&lt;0.0001). The homeopathic treatment resulted in freedom from complaints in 90.3% of the patients and improvement in a further 8.3%, whereas in the placebo group, the complaints remained unchanged or became worse in 88.9% of the patients. Only one adverse event occurred in one patient from the placebo group.</td>
</tr>
</tbody>
</table>
**Sinusitis**

Sinfrontal is a complex homeopathic medication, the efficacy and safety of which has been demonstrated in a number of clinical studies of patients with sinusitis. Sinfrontal was compared with placebo in a cost-utility analysis based on data from a randomized controlled clinical trial over 3 weeks (Sinfrontal group: n = 57; placebo group: n = 56). Sinfrontal led to incremental savings of euro 275 (95% CI 433, 103) per patient compared with placebo over 22 days, essentially due to the markedly reduced absenteeism from work (7.83 vs 12.9 workdays). Incremental utility amounted to 0.0087 QALYs (95% CI 0.0052, 0.0123), or 3.2 quality-adjusted life-days (QALDs). Bootstrapping showed that these findings were significant, with Sinfrontal being dominant in 99.9% of simulations. The results were robust to a number of sensitivity analyses. In the secondary analysis, Sinfrontal led to incremental cost savings of euro 511 and utility gains of 0.015 QALYs or 5.4 QALDs compared with placebo. Compared with antibacterials, Sinfrontal had a significantly higher cure rate (11% vs 59%; p < 0.001) at similar or lower costs. The results of this economic evaluation indicate that Sinfrontal may be a cost-effective treatment for AMS in adults.

<table>
<thead>
<tr>
<th>Study</th>
<th>Condition</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kneis and Gandjour</strong> (2009)</td>
<td>Sinusitis</td>
<td>Sinfrontal was compared with placebo in a cost-utility analysis based on data from a randomized controlled clinical trial over 3 weeks (Sinfrontal group: n = 57; placebo group: n = 56). Sinfrontal led to incremental savings of euro 275 (95% CI 433, 103) per patient compared with placebo over 22 days, essentially due to the markedly reduced absenteeism from work (7.83 vs 12.9 workdays). Incremental utility amounted to 0.0087 QALYs (95% CI 0.0052, 0.0123), or 3.2 quality-adjusted life-days (QALDs). Bootstrapping showed that these findings were significant, with Sinfrontal being dominant in 99.9% of simulations. The results were robust to a number of sensitivity analyses. In the secondary analysis, Sinfrontal led to incremental cost savings of euro 511 and utility gains of 0.015 QALYs or 5.4 QALDs compared with placebo. Compared with antibacterials, Sinfrontal had a significantly higher cure rate (11% vs 59%; p &lt; 0.001) at similar or lower costs. The results of this economic evaluation indicate that Sinfrontal may be a cost-effective treatment for AMS in adults.</td>
</tr>
<tr>
<td><strong>Weiser and Clasen</strong> (1994)</td>
<td>Sinusitis</td>
<td>155 patients with chronic sinusitis received either Euphorbium compositum nasal spray or a placebo to spray twice into each nostril four times a day for 5 months. The verum produced significantly better results.</td>
</tr>
<tr>
<td><strong>Wiesenauer et al.</strong> (1989)</td>
<td>Sinusitis</td>
<td>In the first 7 days Sinfrontal reduced symptoms more than placebo (p&lt;0.0001), and at 3 wks 68% of verum patients were in complete remission compared with 9% on placebo Rx.</td>
</tr>
</tbody>
</table>
### 2.2. Multiple human RCTs in conditions with a tentatively positive direction of evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Condition</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baillargeon et al. (1993)</td>
<td>Blood coagulation</td>
<td>This study adds evidence that antimony 6x significantly increases Maximal Clot Firmness and decreases Clotting Time. The in vivo application of antimony 6x is safe.</td>
</tr>
<tr>
<td>Heusser et al. (2009)</td>
<td>Blood coagulation</td>
<td>Thi s study adds evidence that antimony 6x significantly increases Maximal Clot Firmness and decreases Clotting Time. The in vivo application of antimony 6x is safe.</td>
</tr>
<tr>
<td>Kundu et al. (2012)</td>
<td>Blood coagulation</td>
<td>Homeopathic medicines improved frequency and extent of bleeding, blood products infused, and pain scores (p&lt;0.0001)</td>
</tr>
<tr>
<td>Jacobs et al. (1993)</td>
<td>Childhood diarrhoea</td>
<td>81 children randomised and significant decrease in duration of diarrhoea, and in the number of stools/day after 72 hrs treatment.</td>
</tr>
<tr>
<td>Jacobs et al. (1994)</td>
<td>Childhood diarrhoea</td>
<td>81 children randomised and significant decrease in duration of diarrhoea, and in the number of stools/day after 72 hrs treatment.</td>
</tr>
<tr>
<td>Jacobs et al. (2000)</td>
<td>Childhood diarrhoea</td>
<td>116 children completed treatment. The mean number of stools per day over the entire 5-day treatment period was 3.2 for the treatment group and 4.5 for the placebo group (P = 0.023). A Kaplan-Meier survival analysis of the duration of diarrhoea, which included data from all patient visits, showed an 18.4% greater probability that a child would be free of diarrhoea by day 5 under homeopathic treatment (P = 0.036).</td>
</tr>
<tr>
<td>Jacobs et al. (2006)</td>
<td>Childhood diarrhoea</td>
<td>Homeopathy group did significantly better than the physiotherapy group.</td>
</tr>
<tr>
<td>Gmunder and Kissling (2002)</td>
<td>Low back pain</td>
<td>161 patients Rx for 1 week with a homeopathic gel (SRL) or a Capsicum-based gel (CCC). The two treatments were equally effective, but the homeopathic gel was better tolerated.</td>
</tr>
<tr>
<td>Stam et al. (2001)</td>
<td>Low back pain</td>
<td>Gripp-Heel was as effective as aspirin in treating the common cold on assessments on days 4 &amp; 10</td>
</tr>
<tr>
<td>de Lange de Klerk et al. (1994)</td>
<td>Upper respiratory tract infections</td>
<td>There was a significant difference in median total symptom score in favour of homeopathic care (24 points) compared to the control group (44 points) (0.026). The difference in the median number of days with URTI symptoms was statistically significant with 8 days in the homeopathic group and 13 days in the control group (p 0.006). There was no statistical difference in the use of conventional medication or care between the two groups.</td>
</tr>
<tr>
<td>Maiwald et al. (1988)</td>
<td>Upper respiratory tract infections</td>
<td>Cobalt 30, Causticum 30 &amp; placebo arms. Reaction index was lower in both verum groups than placebo.</td>
</tr>
<tr>
<td>Steinsbekk et al. (2005a)</td>
<td>Upper respiratory tract infections</td>
<td>Both treatments improved vertigo status, and Vertigoheel was not inferior to G. biloba.</td>
</tr>
<tr>
<td>Steinsbekk et al. (2005b)</td>
<td>Upper respiratory tract infections</td>
<td>The differences of the scores of the Index of Total Severity during Radiotherapy trended towards a better activity of the homeopathic medicine and during recovery increased to statistically significance. The homeopathic medicines had particular effectiveness on the heat of the skin.</td>
</tr>
<tr>
<td>Bazzarini et al. (2000)</td>
<td>Radiodermatitis</td>
<td>Cobalt 30, Causticum 30 &amp; placebo arms. Reaction index was lower in both verum groups than placebo.</td>
</tr>
<tr>
<td>Kulkarni et al. (1988)</td>
<td>Radiodermatitis</td>
<td>Both treatments improved vertigo status, and Vertigoheel was not inferior to G. biloba.</td>
</tr>
<tr>
<td>Issing et al. (2005)</td>
<td>Vertigo</td>
<td>This was a study with 119 subjects with various types of vertigo, half of whom were given a homeopathic medicine (a combination of four homeopathic medicines) and half were given a leading conventional drug in Europe for vertigo, betahistine hydrochloride. The homeopathic medicines were found to be similarly effective and significantly safer than the conventional control.</td>
</tr>
</tbody>
</table>
2.3. Conditions supported by a single human RCT

<table>
<thead>
<tr>
<th>Study</th>
<th>Condition</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bignamini et al. (1991)</td>
<td>Anal fissure</td>
<td>Double blind placebo controlled trial involving 31 patients who had pathology for an average of 11 months. After 15 days treatment, burning sensation and patients' assessment significantly in favour of homeopathy, and all other parameters also in favour, but to less than significance.</td>
</tr>
<tr>
<td>Riveron-Garrote (1998)</td>
<td>Asthma</td>
<td>In this double blind, placebo controlled trial, 63 asthmatic patients (34 children and 28 adults) participated, 39 of whom were given individualised homeopathic treatment and 24 were given a placebo. In the treated group, 97.4% improved and 2.6% worsened. 87.2% reduced their use of conventional medication. In the placebo group, 12.5% improved, 16.7 stayed the same, and 70.8% worsened. None of the subjects given a placebo reduced their conventional medication.</td>
</tr>
<tr>
<td>Chapman et al. (1999)</td>
<td>Brain injury</td>
<td>Data from the 50 subjects demonstrated significant reductions in patients' symptom intensity (P&lt;0.01) and difficulty functioning (P=0.0008).</td>
</tr>
<tr>
<td>Diefenbach et al. (1997)</td>
<td>Bronchitis</td>
<td>In a randomised, double-blind placebo-controlled clinical trial, involving 258 patients, the therapeutic effect of the homeopathic combination Bronchiselect was superior; especially the expectoration and dysphagia went better under verum. It is concluded, that the therapy with Bronchiselect is effective.</td>
</tr>
<tr>
<td>Weatherley-Jones et al.</td>
<td>Chronic fatigue syndrome</td>
<td>Individualised homeopathic prescriptions were compared to placebo in 79 people over a 6 month period with monthly observations used to determine clinical progress according to the Multidimensional Fatigue Inventory (MFI) as a primary measure and the Fatigue Impact Scale and Functional Limitations Profile as secondary measures. On the primary MFI measure, those using the individualised homeopathy had significant improvement over placebo.</td>
</tr>
<tr>
<td>Adler et al. (2011)</td>
<td>Depression</td>
<td>There were no significant differences between the percentages of response or remission rates in both groups. Tolerability: there were no significant differences between the side effects rates, although a higher percentage of patients treated with fluoxetine reported troublesome side effects and there was a trend toward greater treatment interruption for adverse effects in the fluoxetine group.</td>
</tr>
<tr>
<td>Katz et al. (2005)</td>
<td>Depression</td>
<td>In this double blind, placebo controlled trial, 63 asthmatic patients (34 children and 28 adults) participated, 39 of whom were given individualised homeopathic treatment and 24 were given a placebo. In the treated group, 97.4% improved and 2.6% worsened. 87.2% reduced their use of conventional medication. In the placebo group, 12.5% improved, 16.7 stayed the same, and 70.8% worsened. None of the subjects given a placebo reduced their conventional medication.</td>
</tr>
<tr>
<td>Egocheaga Rodriguez et al.</td>
<td>Extended sports recovery</td>
<td>Lower blood acidosis and lactic acid was found in the Redimax group than placebo.</td>
</tr>
<tr>
<td>Sharma et al. (2012)</td>
<td>Fracture healing</td>
<td>67 patients with acute non-displaced lateral malleolar fracture. Additional to standard orthopaedic care the treatment group received homeopathic medicine on the basis of totality of symptoms and individualisation. Assessments were taken on 3, 6, 9 and 12 weeks. Faster healing was reported in the homeopathy group by week 9 following injury, including significant improvement in fracture line (p &lt; 0.0001), fracture edge (p&lt;0.0001), callous formation (p&lt; 0.05) and fracture union (p&lt; 0.0001) in comparison to placebo. There was also lower use of analgesics and less self-reported pain in the homeopathy group. The study suggests that homeopathy could enhance anatomical and functional fracture healing.</td>
</tr>
<tr>
<td>Kuzeff (1998)</td>
<td>Immune function</td>
<td>Significant changes were found in 'sensation of well-being' under high potency homeopathic remedy Non significant improvements were noted in CD4 levels.</td>
</tr>
<tr>
<td>Study</td>
<td>Condition</td>
<td>Outcomes</td>
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<tr>
<td>Bernstein et al. (2011)</td>
<td>Non-allergic rhinitis</td>
<td>ICX72 versus placebo subjects exhibited significant differences in symptom changes from baseline to end of study (P &lt; .01), with shorter time to first relief (P &lt; .01), and improvement in nasal congestion, sinus pain, sinus pressure, and headache at 5, 10, 15, and 30 minutes, persisting at 60 minutes for nasal congestion and sinus pain (P &lt; .05). No difference between groups in adverse events or rescue medication was observed. ICX72 versus placebo subjects experienced no rebound congestion or impaired olfaction at the end of the study.</td>
</tr>
<tr>
<td>Colau et al. (2012)</td>
<td>Oral lichen planus</td>
<td>BRN-01 seemed to have a significant effect on the HFS, compared with placebo. According to the results of this clinical trial, BRN-01 may be considered a new therapeutic option with a safe profile for hot flashes in menopausal women who do not want or are not able to take hormone replacement therapy or other recognized treatments for this indication.</td>
</tr>
<tr>
<td>Taylor et al. (2000)</td>
<td>Perennial allergic rhinitis</td>
<td>Fifty patients completed the study. The homoeopathy group had a significant objective improvement in nasal airflow compared with the placebo group (mean difference 19.8 l/min, 95% confidence interval 10.4 to 29.1, P = 0.0001). Initial aggravations of rhinitis symptoms were more common with homoeopathy than placebo (7 (30%) v 2 (7%), P = 0.04). Addition of these results to those of three previous trials (n = 253) showed a mean symptom reduction on visual analogue scores of 28% (10.9 mm) for homoeopathy compared with 3% (1.1 mm) for placebo (95% confidence interval 4.2 to 15.4, P = 0.0007).</td>
</tr>
<tr>
<td>Clark and Percivall (2000)</td>
<td>Plantar fasciitis</td>
<td>14 patients were randomised and Rx for 14 days, generating a significant difference in favour of the Ruta 30C group.</td>
</tr>
<tr>
<td>Bononi (2000)</td>
<td>Post-operative infection</td>
<td>This homeopathic medicament proved to be equally effective and much less expensive.</td>
</tr>
<tr>
<td>Totonchi and Guyuron (2007)</td>
<td>Post-operative oedema</td>
<td>48 patients received either Arnica (A), methylprednisolone (?), or nothing (C). On postoperative day 2 there was a significant difference for the edema rating (p &lt; 0.0001), with group C demonstrating more swelling compared with groups A and P. In addition, on postoperative day 8, group P demonstrated a significantly larger extent of ecchymosis (p &lt; 0.05) and higher intensity of ecchymosis (p &lt; 0.01) compared with groups A and C. There were no differences in the magnitude of edema by postoperative day 8 among the three groups. When the differences between day 2 and day 8 ratings were considered, groups A and C exhibited significantly more resolution of ecchymosis by day 8 compared with group P (p &lt; 0.05).</td>
</tr>
<tr>
<td>Karow et al. (2008)</td>
<td>Post-operative wound healing</td>
<td>The two Rx were equivalent for wound irritation, &amp; swelling, and patient mobility. Arnica was inferior in respect to pain, although there was no significant difference in analgesic usage during 4 post-op days. Arnica D4 was significantly better tolerated (p=0.049).</td>
</tr>
<tr>
<td>Oberbaum et al. (2005)</td>
<td>Postpartum bleeding</td>
<td>At 72 h postpartum, mean Hb levels remained similar after treatment with homeopathic remedies (12.7 versus 12.4) as compared to a significant decrease in Hb levels in the placebo group (12.7 versus 11.6; p&lt;0.05), in spite of less favorable initial characteristics of the treatment group. The mean difference in Hb levels at 72 h postpartum was -0.29 (95% CI -1.09; 0.52) in the treatment group and -1.18 (95% CI -1.82; -0.54) in the placebo group (p&lt;0.05).</td>
</tr>
<tr>
<td>Berrebi et al. (2001)</td>
<td>Postpartum lactation</td>
<td>The Apis 9 CH and Bryonia 9 CH combination was chosen for its anti-inflammatory and analgesic effects. 71 patients were included in this double-blind placebo-controlled study. All received basic treatment comprising naproxen and fluid restriction. A significant improvement of lactation pain (main criterion of the study) was observed in parturients treated with homeopathy (p&lt;0.02 on D2 and p&lt;0.01 on D4). A similar effect (p&lt;0.05 on D4) was observed for breast tension and spontaneous milk flow. The homeopathic combination studied was therefore effective on the pain of lactation and should be integrated into the therapeutic armamentarium</td>
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<tr>
<td>Study</td>
<td>Condition</td>
<td>Outcomes</td>
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<tr>
<td>Yakir et al. (2001)</td>
<td>Premenstrual syndrome</td>
<td>20 women were randomised. Mean questionnaire scores fell from 0.44 to 0.13 ($P&lt;0.05$) with active treatment, and from 0.38 to 0.34 with placebo (NS). (Between group $P=0.057$). Improvement &gt; 30% was observed in 90% of patients receiving active treatment and 37.5% receiving placebo ($P=0.048$).</td>
</tr>
<tr>
<td>Sharma and Sharma (2012)</td>
<td>Pulmonary tuberculosis recovery</td>
<td>Double blind placebo controlled RCT. After 6 months individualised intervention significant improvement was observed in FEV1 ($p&lt;0.001$), forced vital capacity ($p&lt;0.001$), and FEV1/FVC ratio ($p=0.002$). Symptom scores for cough and breathlessness were significantly lower with homeopathy than with placebo ($p&lt;0.001$). At the end of treatment, patients on homeopathy had increased body weight ($p&lt;0.0001$), and better quality of life ($p=0.05$) compared with placebo ($p=0.003$). Benefits were maintained in the homeopathy group after a year whereas symptoms ($p&lt;0.01$) and impact score ($p&lt;0.001$) deteriorated in placebo. Physicians visits were reduced in the homeopathy group by 58.0% ($p=0.002$) compared to placebo ($p&lt;0.0001$).</td>
</tr>
<tr>
<td>Saruggia and Corghi (1992)</td>
<td>Renal failure</td>
<td>Statistically significant improvements of asthenia ($0.0005$), lethargy ($p=0.013$) and headache ($p=0.02$) were detected on active treatment compared to placebo.</td>
</tr>
<tr>
<td>Smith et al. (2002)</td>
<td>Seborrhoeic dermatitis</td>
<td>After 10 weeks treatment the verum patients improved better than the placebo patients ($p&lt;0.04$). The placebo patients also improved after cross-over ($p&lt;0.01$).</td>
</tr>
<tr>
<td>Frass et al. (2005b)</td>
<td>Sepsis</td>
<td>70 patients were randomised. On day 30, there was non-statistically significantly trend of survival in favour of homeopathy (verum 81.8%, placebo 67.7%, $P=0.19$). On day 180, survival was statistically significantly higher with verum homeopathy (75.8% vs. 50.0%, $P=0.043$).</td>
</tr>
<tr>
<td>Lipman et al. (1999)</td>
<td>Snoring</td>
<td>The treatment is significantly more effective than placebo.</td>
</tr>
<tr>
<td>Oberbaum et al. (2001)</td>
<td>Stomatitis</td>
<td>A total of five patients (33%) in the TRAUMEEL S treatment group did not develop stomatitis compared with only one patient (7%) in the placebo group. Stomatitis worsened in only 7 patients (47%) in the TRAUMEEL S treatment group compared with 14 patients (93%) in the placebo group. The mean area under the curve stomatitis scores were 10.4 in the TRAUMEEL S treatment group and 24.3 in the placebo group. This difference was statistically significant ($P&lt;0.01$).</td>
</tr>
<tr>
<td>Frass et al. (2005a)</td>
<td>Tracheal secretions</td>
<td>50 patients on respirators in ICU were randomised. The amount of tracheal secretions was reduced significantly in the group receiving Kali bid 30 ($p&lt;0.0001$). Extubation could be performed significantly earlier in the verum group ($p&lt;0.0001$). Similarly, length of stay was significantly shorter (4.20 - 1.61 days vs 7.68 - 3.60 days, $p&lt;0.0001$).</td>
</tr>
<tr>
<td>Cavalcanti et al. (2003)</td>
<td>Uraemic pruritus</td>
<td>Review at 15, 30, 45 &amp; 60 days was significantly in favour of the verum treatment group.</td>
</tr>
<tr>
<td>Ernst et al. (1990)</td>
<td>Varicose veins</td>
<td>This study of 61 patients showed a 44% improvement in venous filling time in the homeopathic treated group when compared with placebo.</td>
</tr>
</tbody>
</table>
2.4. Multiple human RCTs in conditions with an unclear direction of evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Condition</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reilly et al. (1994)</td>
<td>Allergic asthma</td>
<td>28 Patients with allergic asthma received either a C30 potency of their principal antigen or placebo complementary to the usual conventional care. Symptom improvement was significantly in favour of verum started within 1 week and persisted for up to 8 weeks (p=0.003), with similar trends in respiratory function and bronchial reactivity tests. A meta-analysis of all 3 trials strengthened the evidence separating this Rx from placebo (p=0.0004).</td>
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<tr>
<td>Baker et al. (2003)</td>
<td>Anxiety</td>
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<tr>
<td>Bonne et al. (2003)</td>
<td>Anxiety</td>
<td></td>
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<tr>
<td>McCutcheon (1996)</td>
<td>Anxiety</td>
<td></td>
</tr>
<tr>
<td>Paris et al. (2012)</td>
<td>Anxiety</td>
<td></td>
</tr>
<tr>
<td>Reilly et al. (1994)</td>
<td>Anxiety</td>
<td></td>
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<tr>
<td>de Freitas et al. (1995)</td>
<td>Childhood asthma</td>
<td></td>
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<tr>
<td>White et al. (2003)</td>
<td>Childhood asthma</td>
<td></td>
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<tr>
<td>Thompson et al. (2011)</td>
<td>Childhood asthma</td>
<td></td>
</tr>
<tr>
<td>Fisher et al. (2006)</td>
<td>Eczema</td>
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<tr>
<td>Siebenwirth et al. (2009)</td>
<td>Eczema</td>
<td></td>
</tr>
<tr>
<td>Bergmann et al. (2000)</td>
<td>Female infertility</td>
<td>The outcome measure being spontaneous menstruation, improved concentration of progesterone in the luteal phase, shortening of the cycle, earlier ovulation, and pregnancy was achieved in 38 out of 67 women. It was achieved more often from women with oligomenorrhea in the Phyto Hypophyson L group compared to the placebo group (82 versus 45%, p = 0.021).</td>
</tr>
<tr>
<td>Gerhard et al. (1998)</td>
<td>Female infertility</td>
<td>Pregnancy or spontaneous menstruation in women with amenorrhoea, and pregnancy or improved concentrations of luteal hormones in both other groups, was achieved in 31 out of 66 women who were suitable for evaluation. It was achieved more often in the Mastodynon group compared to the placebo group (57.6% versus 36.0%, p = 0.069). 15 women conceived during the observation period (n = 7 with amenorrhoea, n = 4 with idiopathic infertility, n = 4 with luteal insufficiency). In women with amenorrhoea or luteal insufficiency, pregnancy occurred in the Mastodynon group more than twice as often as in the placebo group.</td>
</tr>
<tr>
<td>Bignamini et al. (1987)</td>
<td>Hypertension</td>
<td></td>
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<tr>
<td>Campistrous Lavaut (1999)</td>
<td>Hypertension</td>
<td>68 patients in a double-blind RCT with mild to moderate hypertension. Benefit of treatment with individualised homeopathy was significantly better in the verum group.</td>
</tr>
<tr>
<td>Hitzenberger and Rehak (2005)</td>
<td>Hypertension</td>
<td></td>
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<tr>
<td>Hill et al. (1995)</td>
<td>Insect bites</td>
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<tr>
<td>Hill et al. (1996)</td>
<td>Insect bites</td>
<td></td>
</tr>
<tr>
<td>Rahlfis and Mössinger (1976)</td>
<td>IBS</td>
<td>Asafoetida was found to be more effective than placebo (p=0.01) in these 91 patients.</td>
</tr>
<tr>
<td>Study</td>
<td>Condition</td>
<td>Outcomes</td>
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</tr>
<tr>
<td>Colau et al. (2012)</td>
<td>Menopausal symptoms</td>
<td>BRN-01 seemed to have a significant effect on the HFS, compared with placebo. According to the results of this clinical trial, BRN-01 may be considered a new therapeutic option with a safe profile for hot flashes in menopausal women who do not want or are not able to take hormone replacement therapy or other recognized treatments for this indication.</td>
</tr>
<tr>
<td>Jacobs et al. (2005a)</td>
<td>Menopausal symptoms after breast cancer</td>
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<tr>
<td>Thompson et al. (2005)</td>
<td>Menopausal symptoms after breast cancer</td>
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<tr>
<td>Straumsheim et al. (2000)</td>
<td>Migraine</td>
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<tr>
<td>Adkison et al. (2010)</td>
<td>Muscle soreness</td>
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<tr>
<td>Plezbert and Burke (2005)</td>
<td>Muscle soreness</td>
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<tr>
<td>Tuten and McClung (1999)</td>
<td>Muscle soreness</td>
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<tr>
<td>Tveiten et al. (1991)</td>
<td>Muscle soreness</td>
<td>18 participants took Arnica D30 twice daily for 5 days starting the day before the race. Blood tests were taken at race end and 48 and 72 hrs. CK was higher at 48hrs in the placebo group (p=0.07). Sensation of stiffness was higher in placebo group (p=0.06&amp;0.07 on day 2&amp;3).</td>
</tr>
<tr>
<td>Whitmarsh et al. (1997)</td>
<td>Muscle soreness</td>
<td></td>
</tr>
<tr>
<td>Kotlus et al. (2010)</td>
<td>Post-operative bruising</td>
<td>29 patients were randomised and the patients receiving homeopathic A montana were found to have a smaller area of ecchymosis on postoperative days 1, 5, 7, and 10. These differences were statistically significant (P&lt;.05) only on postoperative days 1 (P&lt;.005) and 7 (P&lt;.001).</td>
</tr>
<tr>
<td>Seeley et al. (2006)</td>
<td>Post-operative bruising</td>
<td>Double blind placebo controlled RCT demonstrates aconite is useful in reducing post-op agitation and pain. Aconite proved to be effective for children’s postoperative agitation with 95% good results. It is usually stated in such studies that the placebo effect is high and may reach rates higher than 30%. Aconite is an amazing cure when well prescribed, as much for the speediness of its action as for its efficiency. This remedy has a place in the recovery-room and should be in every physician’s emergency case.</td>
</tr>
<tr>
<td>Albeau and Jobert (1990)</td>
<td>Post-operative pain</td>
<td>In all three trials, patients receiving homeopathic arnica 30x showed a trend towards less postoperative swelling compared to patients receiving placebo. However, a significant difference in favour of homeopathic arnica was only found in the CLR trial.</td>
</tr>
<tr>
<td>Hart et al. (1997)</td>
<td>Post-operative pain</td>
<td></td>
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<tr>
<td>Kaziro (1984)</td>
<td>Post-operative pain</td>
<td></td>
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<tr>
<td>Lokken et al. (1995)</td>
<td>Post-operative pain</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Condition</td>
<td>Outcomes</td>
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<td>-------------------------------</td>
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<tr>
<td>Robertson et al. (2007)</td>
<td>Post-operative pain</td>
<td>Arnica 30 6 times on 1st day and bd for next 7 days was significantly superior to placebo in reducing pain scores from days 1 to 14, but not analgesic consumption.</td>
</tr>
<tr>
<td>Singer et al. (2010)</td>
<td>Post-operative pain</td>
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<tr>
<td>Stevinson et al. (2003)</td>
<td>Post-operative pain</td>
<td></td>
</tr>
<tr>
<td>Wolf et al. (2003)</td>
<td>Post-operative pain</td>
<td></td>
</tr>
<tr>
<td>Andrade et al. (1991)</td>
<td>Rheumatoid arthritis</td>
<td>In this randomised, double-blind clinical trial, 111 people were given either placebo or a combination of homeopathic Berberis, Bryonia Nux vomica and Ledum. Using pain, stiffness, inflammatory signs, fatigue and a functional index to determine clinical outcomes, at the end of the 12 week treatment period it was found that the homeopathic combination provided superior results to those of placebo.</td>
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<tr>
<td>Brien et al. (2011)</td>
<td>Rheumatoid arthritis</td>
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<tr>
<td>Fisher and Scott (2001)</td>
<td>Rheumatoid arthritis</td>
<td></td>
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<tr>
<td>Wiesenauer and Gaus (1991)</td>
<td>Rheumatoid arthritis</td>
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<tr>
<td>Labrecque et al. (1992)</td>
<td>Warts</td>
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<tr>
<td>Manchanda et al. (1997)</td>
<td>Warts</td>
<td>147 patients were treated with remedies in potencies from 30C to 1M for 15 days showed homeopathy superior to placebo.</td>
</tr>
</tbody>
</table>
2.5. Conditions for which there are only single inconclusive RCTs

<table>
<thead>
<tr>
<th>Study</th>
<th>Condition</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>Friese et al. (1997a)</td>
<td>Adenoid vegetations</td>
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<tr>
<td>Belon et al. (2006)</td>
<td>Arsenic toxicity</td>
<td></td>
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<tr>
<td>Schmidt and Ostermayr (2002)</td>
<td>Body weight loss</td>
<td></td>
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<tr>
<td>Gaucher et al. (1994)</td>
<td>Cholera</td>
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<tr>
<td>Mokkapatti (1992)</td>
<td>Conjunctivitis</td>
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<tr>
<td>Jacobs et al. (2007)</td>
<td>Dengue fever symptoms</td>
<td></td>
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<tr>
<td>Walach et al. (1997)</td>
<td>Headache</td>
<td></td>
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<tr>
<td>Rastogi et al. (1999)</td>
<td>HIV</td>
<td></td>
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<tr>
<td>Beer and Heiliger (1999)</td>
<td>Induction of labour</td>
<td></td>
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<tr>
<td>Padilha et al. (2011)</td>
<td>Lead poisoning</td>
<td></td>
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<tr>
<td>van Erp and Brands (1996)</td>
<td>Malaria</td>
<td></td>
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<tr>
<td>Leaman and Gorman (1989)</td>
<td>Minor burns</td>
<td></td>
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<tr>
<td>Wiesenauer and Gaus (1987)</td>
<td>Orthostatic hypotension</td>
<td></td>
</tr>
<tr>
<td>Cornu et al. (2010)</td>
<td>Post-operative bleeding</td>
<td></td>
</tr>
<tr>
<td>Ramelet et al. (2000)</td>
<td>Post-operative haematoma</td>
<td></td>
</tr>
<tr>
<td>Hofmeyr et al. (1990)</td>
<td>Postpartum pain</td>
<td></td>
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<tr>
<td>La Pine et al. (2006)</td>
<td>Shift lag</td>
<td></td>
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<tr>
<td>Simpson et al. (1998)</td>
<td>Tinnitus</td>
<td></td>
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<tr>
<td>Cialdella et al. (2001)</td>
<td>Withdrawal of benzodiazepines</td>
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</tbody>
</table>
### 2.6. Conditions for which there is a single RCT with a tentatively negative direction of evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Condition</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Garrett et al. (1997)</td>
<td>Leg ulcers</td>
<td></td>
</tr>
<tr>
<td>Paris et al. (2008)</td>
<td>Post-operative analgesic intake</td>
<td></td>
</tr>
<tr>
<td>Schwartz et al. (1989)</td>
<td>Post-operative ileus</td>
<td></td>
</tr>
<tr>
<td>Witt et al. (2009a)</td>
<td>Vulvo-vaginal candidiasis</td>
<td></td>
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Clinical evidence for homoeopathy

2.7. Studies in more detail with outcomes and level of evidence for homoeopathy

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<td>Jacobs et al. (2003)</td>
<td>I</td>
<td>Three double blind clinical trials of diarrhea in 242 children ages 6 months to 5 years were analyzed as 1 group. Children were randomized to receive either an individualized homeopathic medicine or placebo to be taken as a single dose after each unformed stool for 5 days. Parents recorded daily stools on diary cards, and health workers made home visits daily to monitor children. The duration of diarrhea was defined as the time until there were less than 3 unformed stools per day for 2 consecutive days. A meta-analysis of the effect-size difference of the three studies was also conducted.</td>
<td>Results. Combined analysis shows duration of diarrhea of 3.3 days in the homeopathy group compared with 4.1 in the placebo group ($P = 0.008$). The meta-analysis shows a consistent effect size difference of 0.66 day ($P = 0.008$). Conclusions. The results from these studies confirm that individualized homeopathic treatment decreases the duration of acute childhood diarrhea and suggest that larger sample sizes be conducted.</td>
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<td>Nuhn et al. (2010)</td>
<td>I</td>
<td>It has been hypothesised that randomised, placebo-controlled clinical trials (RCTs) of classical (individualised) homeopathy often fail because placebo effects are substantially higher than in conventional medicine. To compare placebo effects in clinical trials on homeopathy to placebo effects on trials of conventional medicines. We performed a systematic literature analysis on placebo-controlled double-blind RCTs on classical homeopathy. Each trial was matched to three placebo-controlled double-blind RCTs from conventional medicine (mainly pharmacological interventions) involving the same diagnosis. Matching criteria included severity of complaints, choice of outcome parameter, and treatment duration. Outcome was measured as the percentage change of symptom scores from baseline to end of treatment in the placebo group. 35 RCTs on classical homeopathy were identified. 10 were excluded because no relevant data could be extracted, or less than three matching conventional trials could be located.</td>
<td>In 13 matched sets the placebo effect in the homeopathic trials was larger than the average placebo effect of the conventional trials, in 12 matched sets it was lower ($P = 0.39$). Additionally, no subgroup analysis yielded any significant difference. Conclusions: Placebo effects in RCTs on classical homeopathy did not appear to be larger than placebo effects in conventional medicine.</td>
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<td>Posadzki et al. (2012)</td>
<td>I</td>
<td>The aim of this systematic review was to critically evaluate the evidence regarding the adverse effects (AEs) of homeopathy. Method: Five electronic databases were searched to identify all relevant case reports and case series.</td>
<td>In total, 38 primary reports met our inclusion criteria. Of those, 30 pertained to direct AEs of homeopathic remedies; and eight were related to AEs caused by the substitution of conventional medicine with homeopathy. The total number of patients who experienced AEs of homeopathy amounted to 1159. Overall, AEs ranged from mild-to-severe and included four fatalities. The most common AEs were allergic reactions and intoxications. Rhus toxidendron was the most frequently implicated homeopathic remedy. Homeopathy has the potential to harm patients and consumers in both direct and indirect ways. Clinicians should be aware of its risks and advise their patients accordingly.</td>
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There are conceptual and historical links between homeopathic medicine and modern allergy desensitization treatment. Conventional allergy desensitization and homeopathic treatment both utilize small doses of substances that might cause symptoms in order to prevent or treat a hypersensitive state. Homeopathy has historically been associated with allergy treatment. This article reviews evidence from controlled trials for the use of homeopathy in respiratory allergies. Several clinical trials, many of which were published in "high impact" conventional medical journals, describe significant effects of homeopathic treatment in allergic patients. Most of these clinical studies have been deemed to be high quality trials, according to the three most commonly referenced meta-analyses of homeopathic research. Basic in vitro experimental studies also provide evidence that the effects of homeopathy differ from placebo.

Research outcomes considered to be highest in the hierarchy of evidence are mostly negative or inconclusive, whereas all others are positive. This clearly identified trend is analysed against trial designs and treatments strategy. It was found that usually the designs of RCTs limit the full evaluation of the effect of a homeopathic prescription and recommendations for future trials and research designs are made. The encouraging findings for homeopathy coming from well-constructed RCTs and observational studies should be considered more seriously and more trials and studies are recommended in order to replicate such findings.

Elevated levels of ESR, creatinine and eosinophils and increased activities of AST, ALT, LPO and GGT were recorded in arsenic exposed subjects. Decreased levels of hemoglobin, PCV, neutrophil percentages, and GSH content and low G-6-PD activity were also observed in the arsenic exposed people. The administration of "verum" appeared to make positive modulations of these parameters, suggestive of its ameliorative potentials. Most of the subjects reported better appetite and improvement in general health, thereby indicating possibility of its use in remote arsenic-contaminated areas as an interim health support measure to a large population at risk.

Mercury Intoxication: High Dilution as Mercury’s Chelating Agent. The aim was to evaluate the effect of homeopathically prepared mercury on mercury elimination in humans. 52 people suffering from mercury intoxication were randomly assigned to receive the homeopathically prepared mercury (Merc sol) or a placebo. Quality of life assessments and mercury in blood, urine and hair tests were made a priori, at 30 and 60 days. It was found that the verum significantly decreased mercury in hair, with indication of increase in urinary elimination and improvement in symptomatology.

Those patients in the control group experienced a reduction in migraine frequency from 9.9 attacks per month to 7.9 per month, while those in the treatment group reduced their monthly attack rate from 10 to between 1.8 and 3 per month.
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<td>Colau et al. (2012)</td>
<td>II</td>
<td>Homeopathic medicines have a place among the non-hormonal therapies for the treatment of hot flashes during the menopause. Objective: The objective of this study was to evaluate the efficacy of the non-hormonal treatment BRN-01 in reducing hot flashes in menopausal women. This was a multicenter, randomized, double-blind, placebo-controlled study carried out between June 2010 and July 2011. The study was conducted in 35 active centers in France (gynecologists in private practice). One hundred and eight menopausal women, 50 years of age, were enrolled in the study. The eligibility criteria included menopause for &lt;24 months and 5 hot flashes per day with a significant negative effect on the women's professional and/or personal life.</td>
<td>The main outcome measure was the hot flash score (HFS) compared before, during, and after treatment. Secondary outcome criteria were the quality of life (QoL) [measured using the Hot Flash Related Daily Interference Scale (HFRDIS)], severity of symptoms (measured using the Menopause Rating Scale), evolution of the mean dosage, and compliance. All adverse events (AEs) were recorded. One hundred and one women were included in the final analysis (intent-to-treat population: BRN-01, n=50; placebo, n=51). The global HFS over the 12 weeks, assessed as the area under the curve (AUC) adjusted for baseline values, was significantly lower in the BRN-01 group than in the placebo group (mean±SD 88.2±6.5 versus 107.2±6.4, p=0.0411). BRN-01 was well tolerated; the frequency of AEs was similar in the two treatment groups, and no serious AEs were attributable to BRN-01. BRN-01 seemed to have a significant effect on the HFS, compared with placebo. According to the results of this clinical trial, BRN-01 may be considered a new therapeutic option with a safe profile for hot flashes in menopausal women who do not want or are not able to take hormone replacement therapy or other recognized treatments for this indication.</td>
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<td>Dorfman et al. (1987)</td>
<td>II</td>
<td>In a randomised double blind trial involving 93 women, a combination (complex) of Caulophyllum, Actaea racemosa, Arnica montana, Pulsatilla pratensis and Gelsemium sempervirens, all in 5C potencies, was used from the ninth month of pregnancy and its effect on the length of labor and complication rates examined.</td>
<td>The average time of labor was reduced to 5.1 hours while, in comparison, the placebo was associated with an average labor time of 8.5 hours. The rate of complications for those using the homoeopathic complex was 11.3% while the complication rate under placebo was 40%. Complex and routine prescribing, as done in this study, is recognised as amateurish homeopathy so it is reasonable to think that individualised prescribing according to each woman's symptoms would have produced results of even further significance.</td>
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<td>Hellhammer and Schubert (2012)</td>
<td>II</td>
<td>Stress impacts on health, causing stress-related illness. The aim of this study was to investigate stress-dampening effects of the homeopathic combination remedy dysto-logs(®) S on physiological and psychological measures during acute stress. Additionally, effects of the substance on sleep and life quality were investigated. This randomized, double-blind, placebo-controlled single center study had a total duration of 15 days for each participant. Included 40 women aged 30-50 years that regularly experienced impaired well-being when feeling stressed. Participants took three tablets daily for 14 days. On the final study day, participants took three pills in the morning and upon arrival at the study site. Thereafter, the Trier Social Stress Test (TSST) was performed. Primary endpoints were saliva cortisol responses to the stress test. Secondary biological endpoints were plasma cortisol, adrenocorticotrophic hormone, epinephrine, and norepinephrine (NE) and heart rates. Psychological secondary endpoints were well-being, anxiety, stress, and insecurity during the stress test as well as sleep and quality of life.</td>
<td>Stress-induced cortisol levels did not differ between groups, but verum-treated participants were characterized by lower NE levels. Two weeks of treatment with the homeopathic substance resulted in a better sleep quality. Sleep improvement was associated with a higher hormonal response to the TSST in both groups. In addition, individuals with impaired sleep in the placebo group had higher unstimulated NE levels. This study provides preliminary evidence for beneficial effects of dystologes S on sleep quality. Improvement of sleep quality was positively associated with a normalized neuroendocrine stress response during acute stress, whereas an altered hormonal response was observed in participants with impaired sleep. We hypothesize that the test product may possibly reduce NE release.</td>
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<td>Katz et al. (2005)</td>
<td>II</td>
<td>To assess the feasibility of a general practice-based clinical trial comparing the effectiveness of individualised homeopathic treatment vs Fluoxetine (Prozac) vs placebo in the treatment of major depressive episodes of moderate severity. DESIGN: Randomised, double-dummy, double-blind parallel group clinical trial.</td>
<td>31 patients were referred, 23 met the entry criteria, 11 were randomised &amp; 6 completed the study - 1 on homeopathy, 2 placebo &amp; 3 Floxetine. A trial of this design in general practice is not feasible, because of recruitment difficulties, many of them linked to patient preference.</td>
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<td>Kneis and Gandjour (2009)</td>
<td>II</td>
<td>Sinfrontal, a complex homeopathic medication, is popular in Germany for the treatment of ear, nose and throat infections and respiratory tract infections. The efficacy and safety of Sinfrontal has been demonstrated in a number of clinical studies of patients with sinusitis. To assess the cost effectiveness of Sinfrontal versus placebo in the treatment of adults with acute maxillary sinusitis (AMS) in Germany. A secondary objective was to assess the cost effectiveness of Sinfrontal versus standard treatment with antibacterials. Sinfrontal was compared with placebo in a cost-utility analysis based on data from a randomized controlled clinical trial over 3 weeks (Sinfrontal group: n = 57; placebo group: n = 56). Trial data were analysed from a societal perspective; resource use was valued with German unit costs for 2005. In a secondary analysis, the longer-term cost utility of Sinfrontal versus placebo was estimated over a total of 11 weeks based on an 8-week post-treatment observational phase. In addition, the cost effectiveness of Sinfrontal versus antibacterials was determined based on an indirect comparison of placebo-controlled trials.</td>
<td>Sinfrontal led to incremental savings of €275 (95% CI 433, 103) per patient compared with placebo over 22 days, essentially due to the markedly reduced absenteeism from work (7.83 vs 12.9 workdays). Incremental utility amounted to 0.0087 QALYs (95% CI 0.0052, 0.0123), or 3.2 quality-adjusted life-days (QALDs). Bootstrapping showed that these findings were significant, with Sinfrontal being dominant in 99.9% of simulations. The results were robust to a number of sensitivity analyses. In the secondary analysis, Sinfrontal led to incremental cost savings of €511 and utility gains of 0.015 QALYs or 5.4 QALDs compared with placebo. Compared with antibacterials, Sinfrontal had a significantly higher cure rate (11% vs 59%; p &lt; 0.001) at similar or lower costs. The results of this economic evaluation indicate that Sinfrontal may be a cost-effective treatment for AMS in adults.</td>
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<td>Kulkarni et al.</td>
<td>II</td>
<td>RCT in cancer patients to assess the effectiveness of homeopathy on the severity of radio-therapy-related side effects. Patients with different types of cancer were randomized into three parallel arms: placebo; cobaltum 30; and causticum 30 (types of dilution were not specified). These homeopathic remedies were selected because they mimic various symptoms of radiation reaction. All the patients were evaluated once a week according to an 18-point radiation reaction profile, and the average grading was calculated at the end of the study: 0-5 for minimal reaction; 6-10 for moderate but tolerable reaction; and &gt;11 for severe degree of reaction.</td>
<td>Reaction index was lower in both intervention groups compared to placebo (5 for homeopathic groups vs. 8.5 for placebo group). No significant differences in tumour reduction were observed in the study.</td>
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<td>Kundu et al.</td>
<td>II</td>
<td>To investigate the effectiveness of individualised homeopathic medicines in reducing the requirement of factor concentrates in haemophilia patients. In a single blind placebo controlled cross over trial 28 consecutive persons with haemophilia (PWH) with severe (24) or moderately severe (4) disease received standard management with placebo homeopathy for 1 year and active homeopathic treatment in the subsequent year with the same conventional management. There was no wash out period. They received standard managements for any acute emergency during the study period. Development of inhibitor during the study period was a withdrawal criterion. Sample size for the trial was calculated as 24 PWH. Transfusion requirements, bleeding scores, pain scores were evaluated blind by independent experts. Homeopathic medicines were selected by experienced homeopathic physicians depending on clinical condition of the patient. Chi-squared and paired t tests were used in statistical analysis.</td>
<td>28 patients were recruited. Homeopathic medicines improved frequency of bleeding, extent of bleeding, blood products consumed and pain scores (P&lt;0.0001). There was also significant improvement in well being. Plasma levels of clotting factors did not change. No patients developed inhibitors during the study there were no dropouts. Individualised homeopathic medicines may have an important supportive role in the management of PWH, where blood products and factor concentrates are not easily available. Larger, perhaps multi-centric trials are warranted.</td>
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<td>Lyrio et al.</td>
<td>II</td>
<td>The use of homeopathy to prevent symptoms of human flu and acute respiratory infections: a double blind, randomized, placebo-controlled clinical trial with 600 children from Brazilian Public Health Service. A homeopathy clinical trial, employing a control protocol (double-blind, randomized, placebo-controlled), was developed, starting in April 2009 and ending in April 2010. This clinical trial aimed to evaluate the efficacy of two types of biotherapics to prevent symptoms of both flu and acute respiratory infections, compared to placebo (ethanol 30%). The biotherapics tested were ARI (Acute Respiratory Infection) and InfluBio. ARI is a homeopathic complex containing three different microorganisms related to respiratory infection while InfluBio is a biotherapeutic compounded from infectious influenza A virus. Nosodes of potential infecting agents or placebo were given to 600 children age 1-5yrs daily for 30 days.</td>
<td>Of the 600 children, 450 completed the planned monitoring. The main 150 Reasons Why quit the treatment were change of address and parents’ abandonment. In the case of the children who received placebo, the frequency of the acute respiratory episodes Diagnosed infection / flu was three times higher When Compared to Those That ARI and InfluBio received the samples, considering the upper limit of the interquartile interval. Moreover, these children Treated with biotherapics did not present any or presented only a single episode of ARI / flu. These results Showed That ambos biotherapics tested were statistically higher (p &lt;0.01) than placebo, ie, the frequency of the minimized biotherapics symptomatic episodes of flu. Besides the efficacy of homeopathic medicines PROVED, the homeopathic treatment presents the additional advantages include That the low cost of medicine and the compounding Absence of adverse effects registered, Which put this as a very useful therapeutic option for the Public Health Service</td>
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<td>Manchanda et al. (1997)</td>
<td>II</td>
<td>This trial was reported in two parts, one to evaluate the efficacy of homeopathy for warts (remedies included Ruta graveolens, Nitricum acidum, Dulcamara, Causticum and Thuja) the other to evaluate the homoepathic remedy, Calcarea carbonica, for Molluscum contagiosum.</td>
<td>Placebo controlled studies involving a total of 147 subjects using single remedies in 30C potencies three times daily, 200C twice daily and 1M daily, for 15 days, showed that homoeopathy was superior to placebo. Thuja was the most successful of the remedies used for warts</td>
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<td>Sharma and Sharma (2012)</td>
<td>II</td>
<td>Previous studies show that treated and cured pulmonary tuberculosis patients do suffer from pulmonary impairment, lower health related quality of life, disability and long term morbidity, thus responsible for a majority of the disease burden. Despite this, no effective management is available for most of the patients. Therefore, the present study was undertaken to evaluate the impact of homeopathy on pulmonary, functional and quality of life status of patients with pulmonary tuberculosis who have completed treatment. Patients who were cured and had completed anti-tuberculosis treatment within a period of 5 years were enrolled in a randomized double-blind placebo-controlled trial. Individualised homeopathy treatment was given to 61 patients and identical placebo to 57 patients. Symptomatic changes, pulmonary function tests, and health related quality of life were assessed prior to treatment, after 6 months of intervention, and followed up for a year after completing the intervention.</td>
<td>Double blind placebo controlled RCT. After 6mths individualised intervention significant improvement was observed in FEV1 (p&lt;0.001), forced vital capacity (p&lt;0.001), and FEV1/FVC ratio (p=0.002). Symptom scores for cough and breathlessness were significantly lower with homeopathy than with placebo (p&lt;0.001). At the end of treatment, patients on homeopathy had increased body weight (p&lt;0.0001), and better quality of life (p&lt;0.05) compared with placebo (p=0.003). Benefits were maintained in the homeopathy group after a year whereas symptoms (p&lt;0.01) and impact score (p&lt;0.001) deteriorated in placebo. Physicians visits were reduced in the homeopathy group by 58.0% (p =0.002) compared to placebo (p&lt;0.0001). Homeopathy is effective in improving lung capacity and health status. Benefits remain evident after a year. This suggests that homeopathy could make an important contribution to post treatment tuberculosis pulmonary impairment</td>
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<td>Sharma et al. (2012)</td>
<td>II</td>
<td>In clinical practice, homeopathy is widely used in the fracture-repair process, which accelerates the healing of fractures, enhances callus formation and reduces pain. But there is no anatomical or scientific evidence yet to prove that. Therefore, the current study was undertaken to test the efficacy of homoeopathy in bone fracture healing. The study was conducted as a double blind randomized controlled study with 67 patients with acute non-displaced lateral malleolar fracture. Patients were recruited from the Emergency Orthopaedic department, SMS Hospital, Jaipur, India during May 2007 to May 2009. Patients were randomized to either a homoeopathy treatment (n=34) or a control group (n=33). All the patients received standard orthopaedic care through 12 weeks following injury. The treatment group received homoeopathic medicine on the basis of totality of symptoms and individualisation. Outcome measures include radiological assessments and functional tests for healing. Assessments were taken on 3, 6, 9 and 12 weeks.</td>
<td>Faster healing was reported in the homoeopathy group by week 9 following injury, including significant improvement in fracture line (p &lt; 0.0001), fracture edge (p&lt;0.0001), callous formation (p&lt; 0.05) and fracture union (p&lt; 0.0001) in comparison to placebo. There was also lower use of analgesics and less self-reported pain in the homoeopathy group.</td>
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<td>Sinha et al. (2012)</td>
<td>II</td>
<td>To compare the effectiveness of Homeopathy and Conventional therapy in Acute Otitis Media (AOM). A randomized placebo-controlled parallel group pilot study of homeopathic vs conventional treatment for AOM was conducted in Jaipur, India. Patients were randomized by a computer generated random number list to receive either individualized homeopathic medicines in fifty millesimal (LM) potencies, or conventional treatment including analgesics, antipyretics and anti-inflammatory drugs. Patients who did not improve were prescribed antibiotics at the 3rd day. Outcomes were assessed by the Acute Otitis Media-Severity of Symptoms (AOM-SOS) Scale and Tympanic Membrane Examination over 21 days.</td>
<td>81 patients were included, 80 completed follow-up: 41 for conventional and 40 for homeopathic treatment. In the Conventional group, all 40 (100%) patients were cured, in the Homeopathy group, 38 (95%) patients were cured while 02 (5%) patients were lost to the last two follow-up. By the 3rd day of treatment, 4 patients were cured in Homeopathy group but in Conventional group only one patient was cured. In the Conventional group antibiotics were prescribed in 39 (97.5%), no antibiotics were required in the Homeopathy group. 85% of patients were prescribed six homeopathic medicines. Individualized homeopathy is an effective conventional treatment in AOM, there were no significant differences between groups in the main outcome. Symptomatic improvement was quicker in the Homeopathy group, and there was a large difference in antibiotic requirements, favouring homeopathy. Further work on a larger scale should be conducted.</td>
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<td>Wiesenauer et al. (1983)</td>
<td>II</td>
<td>Until now the therapy of pollinosis with Galphimia glauca was based on individual experience. We performed a randomized, controlled, multicenter, and double-blind clinical trial to verify the effectiveness of the Galphimia glauca D4 therapy of patients with pollinosis. The average time of observation was 51/2 weeks.</td>
<td>Galphimia was found to be more effective than placebo at a 1% level of significance. Therapeutic success was given in 34/41 (= 83%) of the patients with Galphimia and in 21/45 (= 47%) of the control patients</td>
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<td>Fisher (1986)</td>
<td>III-1</td>
<td>An experimental double-blind clinical trial method in homeopathy. Use of a limited range of remedies to treat fibrositis. 24 patients were prescribed for 3 months, according to indication, one of three homeopathic remedies (Arnica, Bryonia, Rhus tox.), each patient remaining on the same remedy throughout. They were followed monthly on the following parameters: pain, number of tender spots and sleep. An 'indication score' was allotted to each prescription.</td>
<td>The results were analyzed by non-parametric statistical methods, showing that homœopathy produced a statistically significant improvement, but only when the prescribed remedy was well indicated.</td>
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<td>Gibson et al. (1980)</td>
<td>III-1</td>
<td>Homoeopathic Therapy in Rheumatoid Arthritis: Evaluation by Double Blind Clinical Therapeutic Trial. Twenty-three patients with rheumatoid arthritis on orthodox first-line anti-inflammatory treatment plus homeopathy were compared with a similar group of twenty-three patients on orthodox first-line treatment plus an inert preparation.</td>
<td>There was a significant improvement in subjective pain, articular index, stiffness and grip strength in those patients receiving homoeopathic remedies whereas there was no significant change in the patients who received placebo. Two physicians were involved in prescribing for the patients and there were no significant differences in the results which they obtained. No side effects were observed with the homoeopathic remedies.</td>
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<td>Albertini et al. (1985)</td>
<td>III-2</td>
<td>Homeopathic treatment of dental neuralgia by Amica and Hypericum</td>
<td>Arnica 7C alternated with Hypericum 15C every 4hrs over 3 days in 30 patients with neuralgia after tooth extraction was successful with 23, compared with 12 of 30 patients given placebo.</td>
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<td>Ammerschlager et al. (2005)</td>
<td>III-2</td>
<td>Treatment of inflammatory diseases of the upper respiratory tract – comparison of a homeopathic complex remedy with xylometazoline</td>
<td>Comparable efficacy and tolerability profile of the homeopathic complex remedy Euphorbium compositum nasal drops SN and the reference substance xylometazoline in the treatment of inflammatory diseases of the upper respiratory tract.</td>
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<td>Banerjee et al. (2010a)</td>
<td>III-2</td>
<td>Can Homeopathy Bring Additional Benefits to Thalassemic Patients on Hydroxyurea Therapy? Encouraging Results of a Preliminary Study.</td>
<td>Several homeopathic remedies, namely, Pulsatilla Nigricans (30th potency), Ceanothus Americanus (both mother tincture and 6th potency) and Ferrum Metallicum (30th potency) selected as per similia principles were administered to 38 thalassemic patients receiving Hydroxyurea (HU) therapy for a varying period of time. Levels of serum ferritin (SF), fetal hemoglobin (HbF), hemoglobin (Hb), platelet count (PC), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), white blood cell (WBC) count, bilirubin content, alanine amino transferase (ALT), aspartate amino transferase (AST) and serum total protein content of patients were determined before and 3 months after administration of the homeopathic remedies in combination with HU to evaluate additional benefits, if any, derived by the homeopathic remedies, by comparing the data with those of 38 subjects receiving only HU therapy. Preliminary results indicated that there was a significant decrease in the SF and increase in HbF levels in the combined, treated subjects. Although the changes in other parameters were not so significant, there was a significant decrease in size of spleen in most patients with splenomegaly and improvement in general health conditions along with an increased gap between transfusions in most patients receiving the combined homeopathic treatment. The homeopathic remedies being inexpensive and without any known side-effects seem to have great potentials in bringing additional benefits to thalassemic patients; particularly in the developing world where blood transfusions suffer from inadequate screening and fall short of the stringent safety standards followed in the developed countries. Further independent studies are encouraged.</td>
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<td>Bononi (2000)</td>
<td>III-2</td>
<td>Echinacea comp. Forte S in the prophylaxis of post-operative infections. A comparative study versus ceftazidime and ceftriaxone.</td>
<td>This homeopathic medicament proved to be equally effective and much less expensive.</td>
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<td>Derasse et al. (2005)</td>
<td>III-2</td>
<td>The effects of a complex homeopathic medicine compared with acetaminophen in the symptomatic treatment of acute febrile infections in children: an observational study.</td>
<td>198 children suffering from acute febrile infections were treated in 38 Belgian clinics with either acetaminophen or a combination of homeopathic medicines Gripp-Heel. Their symptoms (including fever, cramps, disturbed sleep, crying, and difficulties eating or drinking) were assessed and graded for a response to their respective medicines. It was found that the homeopathic combination was as effective as acetaminophen and the homeopathic medicines were better tolerated.</td>
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<td>Friese et al. (1997b)</td>
<td>III-2</td>
<td>The Homoeopathic Treatment of Otitis Media in Children-comparisons with conventional therapy</td>
<td>103 children, treated by one homoeopath using single homoeopathic remedies (Group A), were compared with 28 children treated by a team of four ear, nose and throat practitioners, using singly or in combination, nasal drops, antibiotics, secretolytics or antipyretics (Group B). The average duration of pain for Group A was 2 days, as opposed to 3 days for Group B. 70.7% of the Group A children were free of recurrences within the first year of treatment and 29% had a maximum of 3 recurrences while in Group B, 56.5% were free of recurrences within the first year of treatment and 43.5% had a maximum of 6 recurrences. Authors concluded that homoeopathic treatment of otitis media offers a safe and effective alternative treatment to conventional treatment with antibiotics.</td>
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<td>Gassinger et al. (1981)</td>
<td>III-2</td>
<td>53 outpatients suffering from common cold (flu) were randomly assigned to either a therapy with acetylsalicylic acid (ASA) or the homeopathic drug Eupatorium perfoliatum D2 in a controlled clinical trial. The efficacy of the drugs was assessed on day 1, 4 and 10 of the infection by symptom check lists and physical examinations</td>
<td>Eupatorium was found to be equally as effective as aspirin for treating the common cold.</td>
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<td>Gibson et al. (1978)</td>
<td>III-2</td>
<td>Salicylates and Homoeopathy in Rheumatoid Arthritis.</td>
<td>41 people were treated with enteric coated aspirin and 54 were treated with individualised homeopathic treatment. The homeopathic treatment was considerably more effective than the aspirin. In addition, 16 of the 41 people taking aspirin during the trial experienced side effects while those taking homeopathics experienced no side effects.</td>
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<td>Haidvogl et al. (2007)</td>
<td>III-2</td>
<td>Homeopathic and conventional treatment for acute respiratory and ear complaints: A comparative study on outcome in the primary care setting.</td>
<td>Data of 1,577 patients were evaluated in the full analysis set of which 857 received homeopathic (H) and 720 conventional (C) treatments. The majority of patients in both groups reported their outcome after 14 days of treatment as complete recovery or major improvement (H: 86.9%; C: 86.0%; p = 0.0003 for non-inferiority testing). In the per-protocol set (H: 576 and C: 540 patients) similar results were obtained (H: 87.7%; C: 86.9%; p = 0.0019). Further subgroup analysis of the full analysis set showed no differences of response rates after 14 days in children (H: 88.5%; C: 84.5%) and adults (H: 85.6%; C: 86.6%). The unadjusted odds ratio (OR) of the primary outcome criterion was 1.40 (0.89-2.22) in children and 0.92 (0.63-1.34) in adults. Adjustments for demographic differences at baseline did not significantly alter the OR. The response rates after 7 and 28 days also showed no significant differences between both treatment groups. However, onset of improvement within the first 7 days after treatment was significantly faster upon homeopathic treatment both in children (p = 0.0488) and adults (p = 0.0001). Adverse drug reactions occurred more frequently in adults of the conventional group than in the homeopathic group (C: 7.6%; H: 3.1%, p = 0.0032), whereas in children the occurrence of adverse drug reactions was not significantly different (H: 2.0%; C: 2.4%, p = 0.7838).</td>
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<td>Haila et al. (2005)</td>
<td>III-2</td>
<td>Effects of homeopathic treatment on salivary flow rate and subjective symptoms in patients with oral dryness: a randomized trial.</td>
<td>13 of the 15 verum treated patients experienced a significant relief of xerostomia, whereas no such effect was found in the placebo group. Stimulated salivary flow rate was slightly higher with homeopathy than placebo but no consistent changes occurred in salivary immunoglobulin (IgA, IgG) levels. In an open follow-up period those receiving homeopathic medicine continued treatment and the placebo group patients were treated with individually prescribed homeopathic medicines. The symptoms of xerostomia improved in both groups.</td>
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<td>Harrison et al. (1999)</td>
<td>III-2</td>
<td>A randomised comparison of homeopathic and standard care for the treatment of glue ear in children.</td>
<td>At 12 mths, 64% of children receiving homeopathic care had a hearing loss less than 20 dB vs 56% standard care. More homeopathy patients than controls had a normal tympanogram (75 vs 31%, P = 0.015). Referrals to specialists and antibiotic consumption was lower in the homoeopathy group, though differences between groups did not reach statistical significance.</td>
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<tr>
<td>Khuda-Bukhsh et al. (2011a)</td>
<td>III-2</td>
<td>An initial report on the efficacy of a millesimal potency Arsenicum Album LM 0/3 in ameliorating arsenic toxicity in humans living in a high-risk arsenic village. Zhong Xi Yi Jie He Xue Bao.</td>
<td>Blood samples from 14 people living with arsenic contaminated water supply were treated with either Arsenicum Album LM3 or placebo for 2 mths were compared with samples from 18 people living in an arsenic free village. The verum group had positive modulations of a number of parameters of arsenic toxicity.</td>
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<td>Khuda-Bukhsh et al. (2011c)</td>
<td>III-2</td>
<td>A Follow-Up Study on the Efficacy of the Homeopathic Remedy Arsenicum album in Volunteers Living in High Risk Arsenic Contaminated Areas.</td>
<td>96 people continued to take Arsenicum Album 200C for 6 months, 65 till 1 year and 15 among them continued till 2 years. None of the patients on placebo returned for follow-up. Most of the volunteers reported status quo maintained after the improvement they achieved within the first 3 months of homeopathic treatment, in respect of their general health and spirit, and appetite and sleep. A few with skin symptoms and burning sensation, however, improved further. This was supported by the data of toxicity biomarkers, levels of all of which remained fairly within normal range.</td>
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<td>Klopp et al. (2005)</td>
<td>III-2</td>
<td>Microcirculatory effects of a homeopathic preparation in patients with mild vertigo: an intravital microscopic study.</td>
<td>After 12 weeks of treatment with Vertigoheel, patients with vertigo who received the homeopathic preparation exhibited an increased number of nodal points, increased flow rates of erythrocytes in arterioles and venules, increased numbers of cell-wall adhering leucocytes, increased vasomotion and partial oxygen pressure, and a slight reduction in hematocrit vs. baseline. Compared to the control group these differences were statistically significant. The microcirculatory changes were associated with a reduction in the severity of vertigo in the actively treated patients, both as assessed by the treating physician and by the patients themselves.</td>
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<td>Mazzocchi and Montanaro (2012)</td>
<td>III-2</td>
<td>Observational study of the use of Symphytum 5CH in the management of pain and swelling after dental implant surgery.</td>
<td>The addition of Symphytum reduced pain and swelling.</td>
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<tr>
<td>Mousavi et al. (2009a)</td>
<td>III-2</td>
<td>Homeopathic treatment of minor aphthous ulcer: a randomized, placebo-controlled clinical trial.</td>
<td>100 patients blinded significant improvement in pain and ulcer size on days 4 &amp; 6.</td>
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<td>Mousavi et al. (2009b)</td>
<td>III-2</td>
<td>Ignatia in the treatment of oral lichen planus</td>
<td>Single blind placebo controlled RCT preselected patients with lichen planus, who had the psychological characteristics sensitive to Ignatia. Mean lesion sizes and pain measures differed significantly in favour of verum.</td>
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<tr>
<td>Nahler et al. (1998)</td>
<td>III-2</td>
<td>Treatment of osteoarthritis of the knee with a homeopathic medicine - Results of a randomised controlled clinical trial in comparison to hyaluronic acid.</td>
<td>Zeel Comp was of equivalent efficacy, less expensive and mildly better tolerated.</td>
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<td>Rabe et al. (2004)</td>
<td>III-2</td>
<td>Effectiveness and tolerability of a homoeopathic remedy compared with conventional therapy for mild viral infections.</td>
<td>Treatments for mild viral infections are usually directed at providing symptomatic relief. The effectiveness of the homoeopathic remedy Gripp-Heel was compared with that of conventional treatments in a prospective, observational cohort study in 485 patients with mild viral infections and symptoms such as fever, headache, muscle pain, cough or sore throat. As evaluated by the practitioners, the homoeopathic therapy was effective to similar or greater degree than the conventional therapies: 67.9% of patients were considered asymptomatic at the end of Gripp-Heel therapy vs. 47.9% of patients in the control group. Practitioners judged homoeopathic treatments as 'successful' in 78.1% of cases vs. 52.2% for conventional therapies. Tolerability and compliance were good in both treatment groups, with the verdict 'very good' given for 88.9% of patients in the homoeopathic group vs. 38.8% in the conventional treatment group.</td>
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<tr>
<td>Riley et al. (2001)</td>
<td>III-2</td>
<td>Homeopathy and conventional medicine: an outcomes study comparing effectiveness in a primary care setting.</td>
<td>Homeopathy appeared to be at least as effective as conventional medical care in the treatment of patients with upper &amp; lower respiratory tract (including allergies) and ear complaints with demonstrated advantages over conventional care in rapidity of improvement and rate of adverse effects.</td>
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<tr>
<td>Rossignol et al. (2012)</td>
<td>III-2</td>
<td>Impact of physician preferences for homeopathic or conventional medicines on patients with musculoskeletal disorders: results from the EPI3-MSD cohort</td>
<td>Musculo Skeletal Disease patients seen by homeopathic physicians showed a similar clinical progression when less exposed to NSAID in comparison to patients seen in conventional medical practice, with fewer NSAID-related adverse events and no loss of therapeutic opportunity.</td>
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<td>Schmiedel and Klein (2006)</td>
<td>III-2</td>
<td>A complex homeopathic preparation for the symptomatic treatment of upper respiratory infections associated with the common cold: An observational study.</td>
<td>Conventional therapies with antihistamines, antitussives, and non-steroidal anti-inflammatory drugs on upper respiratory symptoms of the common cold were compared in 397 patients with the homoeopathic complex Engystol (Heel). Both treatment regimens provided significant symptomatic relief, and this homoeopathic treatment was noninferior in a noninferiority analysis. Significantly more patients (P &lt; .05) using Engystol-based therapy reported improvement within 3 days (77.1% vs 61.7% for the control group). No adverse events were reported in any of the treatment groups.</td>
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<td>Torres et al. (2001)</td>
<td>III-2</td>
<td>Utilidad de la homeopatia en la prevencion de las crisis asmaticas en el nino</td>
<td>30 children were treated with homeopathy and 30 by conventional medicine. All 60 had a satisfactory clinical course, but the conventional treatment was 10 times more expensive.</td>
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<td>Trichard et al. (2005)</td>
<td>III-2</td>
<td>Pharmacoeconomic comparison between homeopathic and antibiotic treatment strategies in recurrent acute rhinopharyngitis in children</td>
<td>The 'homeopathic strategy' yielded significantly better results than the 'antibiotic strategy' in terms of medical effectiveness in treating rhinopharyngitis (number of episodes of rhinopharyngitis: 2.71 vs 3.97, P&lt;0.001; number of complications: 1.25 vs 1.95, P&lt;0.001), and quality of life (global score: 21.38 vs 30.43, P&lt;0.001), with lower direct medical costs covered by Social Security (88 Euros vs 99 Euros, P&lt;0.05) and significantly less sick-leave (9.5% of parents vs 31.6% of parents, P&lt;0.001).</td>
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<td>van den Meerschaut and Sunder (2009)</td>
<td>III-2</td>
<td>The Homeopathic Preparation Nervoheel N can Offer an Alternative to Lorazepam Therapy for Mild Nervous Disorders.</td>
<td>In an open-label, prospective non-randomized cohort study, Nervoheel N was compared with lorazepam for a maximum of 4 weeks, in 248 patients with insomnia, distress, anxieties, restlessness or burnout and similar nervous conditions ('mild nervous disorders'). The sum of symptom scores improved by 4.4 points with Nervoheel N and by 4.2 points with lorazepam, which was not a significant difference. Both treatments were well tolerated.</td>
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<td>Villanueva et al. (2012)</td>
<td>III-2</td>
<td>Use of homeopathic formula in malnourished children.</td>
<td>Complex of Calc carb, Calc flour and Calc phos all 30C were given for one-year to 50 mal-nourished children. 42 out of 50 children (84%) treated with homeopathy attained normal weight, whereas only 15 out of 49 (30%) of the children in the control group attained normal weight.</td>
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<td>Waldschütz and Klein (2008)</td>
<td>III-2</td>
<td>The Homeopathic Preparation Neurexan® vs. Valerian for the Treatment of Insomnia: An Observational Study</td>
<td>Neuraxan was shown to be as effective as Valerian, and better in some parameters.</td>
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<td>Wolschner et al. (2001)</td>
<td>III-2</td>
<td>Treating Vertigo - Homeopathic Combination Remedy Therapeutically Equivalent to Dimenhydrinate</td>
<td>352 patients Tx with Vertigoheel were compared with 422 patients Tx with Dimenhydrinate over a max of 8 wks. Physician ratings and reduction of the number, duration and intensity of attacks showed the treatments were equivalent.</td>
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<tr>
<td>Zambrano (2000)</td>
<td>III-2</td>
<td>The Effects of a Complex Homoeopathic Preparation on Aerobic Resistance, Aerobic Capacity, Strength and Flexibility</td>
<td>Redimax facilitated better cellular oxygenation, reducing the production of lactic acid as well as recuperation time.</td>
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<td>Bracho et al. (2010)</td>
<td>III-3</td>
<td>Large-scale application of highly-diluted bacteria for Leptospirosis epidemic control.</td>
<td>Cuban medical researchers reported that in late 2007, their annual epidemic of Leptospirosis was prevented by homeopathy. Of the 2,500,000 people given the prophylactic, only ten developed the disease, a marked contrast to the tens of thousands normally infected each year. No lives were lost and the program was highly cost-effective in comparison to traditional and less effective vaccine programs. The protective effect continued into 2008 with an 84% reduction in leptospirosis cases for the treated area. Leptospirosis infections in untreated areas increased by 22%.</td>
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<td>de Souza Nunes (2008)</td>
<td>III-3</td>
<td>Facing the challenge of controlling an outbreak of dengue, the Secretary of Health of the county of Macaé, Rio de Janeiro, Brazil, in early 2007 carried out a &quot;Homeopathy Campaign against Dengue&quot;. 156,000 doses of homeopathic remedy were freely distributed in April and May 2007 to asymptomatic patients and 129 doses to symptomatic patients treated in outpatient clinics, according to the notion of &quot;epidemic genus&quot;. The remedy used was a homeopathic complex against dengue containing Phosphorus 30cH, Crotalus horridus 30cH and Eupatorium perfoliatum 30cH.</td>
<td>The incidence of the disease in the first three months of 2008 fell 93% by comparison to the corresponding period in 2007, whereas in the rest of the State of Rio de Janeiro there was an increase of 128%. While confounding factors were not controlled for, these results suggest that homeopathy may be an effective adjunct in Dengue outbreak prevention.</td>
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<tr>
<td>Eid et al. (1993)</td>
<td>III-3</td>
<td>Applicability of Homoeopathic Caulophyllum thalictroides during labour</td>
<td>22 primipara were given homeopathic Caulophyllum and their deliveries were compared to 34 labours retrospectively selected on the criteria used to select the test subjects. The women who were given the homeopathic remedy laboured by an average of 90 minutes less than the controls.</td>
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<tr>
<td>Frei and Thurneysen (2001a)</td>
<td>III-3</td>
<td>Homeopathy in acute otitis media in children: treatment effect or spontaneous resolution?</td>
<td>230 children with acute otitis media received either homeopathic treatment or placebo. After 12 hours, 72% of those using homeopathy experienced significant relief of symptoms, which was 2.4 times faster than the response to placebo as noted by other researchers.</td>
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<td>Frei and Thurneysen (2001b)</td>
<td>III-3</td>
<td>The purpose of this prospective trial was to assess the efficacy of homeopathy in hyperactive patients and to compare it MPD. The study was performed in a paediatric practice with conventional and homeopathic backgrounds. Children aged 3-17 y, conforming to the DSM-IV criteria for attention deficit hyperactivity disorder (ADHD) with a Conners Global Index (CGI) of 14 or higher were eligible for the study. All of them received an individual homeopathic treatment. When clinical improvement reached 50%, the parents were asked to re-evaluate the symptoms. Those who did not improve sufficiently on homeopathy were changed to MPD, and again evaluated after 3 months. One hundred and fifteen children (92 boys, 23 girls) with a mean age of 8.3 y at diagnosis were included in the study. Prior to treatment the mean CGI was 20.63 (14-30), the mean index of the homeopathy group 20.52 and of the MPD-group 20.94. After an average treatment time of 3.5 months 86 children (75%) had responded to homeopathy, reaching a clinical improvement rating of 73% and an amelioration of the CGI of 55%. Twenty-five children (22%) needed MPD; the average duration of homeopathic (pre-) treatment in this group was 22 months. Clinical improvement under MPD reached 65%, the lowering of the CGI 48%. Three children did not respond to homeopathy nor to MPD, and one left the study. In cases where treatment of a hyperactive child is not urgent, homeopathy is a valuable alternative to MPD. The reported results of homeopathic treatment appear to be similar to the effects of MPD. Only children who did not reach the high level of sensory integration for school had to be changed to MPD. In pre-schoolers, homeopathy appears a particularly useful treatment for ADHD.</td>
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<td>Iannotti and Melo (2012)</td>
<td>III-3</td>
<td>The impact of the medical speciality in primary health-care problem solving in Belo Horizonte, Brazil: homeopaths versus family doctors: a preliminary quantitative study.</td>
<td>Doctors trained in homeopathy were more effective in solving patient's medical problems and requested fewer tests.</td>
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<td>Marian et al. (2008)</td>
<td>III-3</td>
<td>Patient satisfaction and side effects in primary care: An observational study comparing homeopathy and conventional medicine</td>
<td>The main objective of this study is to investigate patient satisfaction and perception of side effects in homeopathy compared with conventional care in a primary care setting. A total of 6778 adult patients received the questionnaire and 3126 responded (46.1%). Statistically significant differences were found with respect to health status (higher percentage of chronic and severe conditions in the homeopathic group), perception of side effects (2-3 times higher percentage of reported side effects in the conventional group) and patient satisfaction (higher percentage of satisfied patients in the homeopathic group).</td>
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<td>Marino (2008)</td>
<td>III-3</td>
<td>This paper describes experiences of the use of homeopathy in the prevention and treatment Dengue fever in São José do Rio Preto, São Paulo, Brazil. May 2001, a single dose of the homeopathic remedy Eupatorium perfoliatum 30cH was given to 40% of residents of the most highly affected neighborhood.</td>
<td>Thereafter, Dengue incidence decreased by 81.5%, a highly significant decrease as compared with neighbourhoods that did not receive homeopathic prophylaxis (p&lt;0.0001). Between April and September 2007, a homeopathic complex composed of Eupatorium perfoliatum, Phosphorus and Crotalus horridus 30cH, given to 20,000 city residents. This trial was aborted prematurely due to national political intervention; therefore, only partial and isolated data could be recorded. However, the results suggest that homeopathy may be effective in the prevention and treatment of Dengue epidemics.</td>
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<tr>
<td>Mroninski et al. (2001)</td>
<td>III-3</td>
<td>‘Meningococcinum Its protective effect against meningococcal disease’.</td>
<td>Brazilian research conducted during an epidemic of the B serotype, demonstrated 95% protection from one dose of Meningococcinum 30 extending over a 6mth period compared with the population who didn't take the dose.</td>
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<td>Rostock et al. (2011)</td>
<td>III-3</td>
<td>Classical homeopathy in the treatment of cancer patients - a prospective observational study of two independent cohorts.</td>
<td>Fatigue and quality of life improved significantly under homeopathic treatment, but sample size was too small to come to conclusions due to inadequate matching.</td>
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<td>Teixeira (2009)</td>
<td>III-3</td>
<td>Study population comprised adults (average age = 30 year-old) with moderate allergic rhinitis (average score = 15/24) an average duration of disease = 14 years in habitual and long-term use of conventional treatments without any alteration in the natural course of the disease.</td>
<td>From 55 randomized patients, 41 completed Phase 1; 21 in the group with homeopathic treatment and 20 in the group treated with placebo; there was average 25% improvement compared with the baseline score without significant difference between both groups. In phase 2 about 70% of patents (n=27) completed 12 months of individualized homeopathic treatment and present 50% improvement regarding baseline clinical score significant by comparison to improvement in Phase 1; 50% (n=20) and 30% (n=13) patients completed 24 and 36 months of homeopathic treatment respectively, with 64% and 72% of improvement regarding baseline clinical score, both significant by comparison to improvement in Phase 1.</td>
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<td>Adler (1999)</td>
<td>IV</td>
<td>Efficacy and Safety of a Fixed-Combination Homeopathic Therapy for Sinusitis</td>
<td>119 patients with sinusitis treated for average of 2 wks. Prior to treatment with a complex 61.3% of patients had severe headaches, but within one week only 16.8% of patients had this complaint reducing to 2.3% after three weeks. Severely obstructed nasal breathing was experienced by 84% of patients prior to treatment, but only 32.8% experienced it after 1 week, and only 4.1% after three weeks. At the end of treatment 81.5% described themselves as symptom-free or significantly improved.</td>
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<td>Badulici et al. (1994)</td>
<td>IV</td>
<td>Immunoglobin relationship in patients with cirrhosis of the liver before and after treatment with Zincum metallicum 5cH.</td>
<td>10 people suffering from Zinc deficiency as determined by atomic absorption spectrophotometry were treated with Zincum metallicum5C. Analysis following this treatment showed a substantial improvement in zinc levels.</td>
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<td>Cairo et al. (2001)</td>
<td>IV</td>
<td>Homeopathy in Cuban epidemic neuropathy: an open clinical trial</td>
<td>All patients had not had the usual response to at least 3 months of vitamin therapy. They were then treated with Carbon sulph and Tabacum in ascending potencies from 12 to 200C over 1 month. 15 patients with optic neuropathy improved 73.3%, and 16 patients with peripheral neuropathy improved 12.5% over 3 months.</td>
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<td>Castellsagu (1992)</td>
<td>IV</td>
<td>Evolution of 26 cases of bronchial asthma with homeopathic treatment.</td>
<td>Of 26 patients with &gt;1yr follow-up 58% were symptom free for &gt;1yr, 23% improved and 19% unchanged.</td>
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<td>Castellsague and Sturza (1998)</td>
<td>IV</td>
<td>Retrospective Study in Asthma,</td>
<td>196 people were treated for asthma with homeopathy. Of the 196, 54 were claimed to have been cured and improvement was seen in a further 117</td>
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<td>Clover (2000)</td>
<td>IV</td>
<td>Patient benefit survey: Tunbridge Wells Homoeopathic Hospital</td>
<td>1372 patients attending a hospital outpatient clinic completed a questionnaire during 1997, grading the degree of change their medical problem, -3(2%), -2(3%), -1(4%), 0(17%), +1(19%), +2(24%), +3(31%).</td>
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<tr>
<td>Clover and Ratsey (2002)</td>
<td>IV</td>
<td>We report an uncontrolled, pilot outcome study, conducted at the Tunbridge Wells Homeopathic Hospital (TWHH) in 1998-1999. The study was conducted in out-patient consultations booked in the usual way. Thirty-one patients referred to the Department for menopausal flushes and seen for an initial consultation and at least one follow-up review, were assessed in three groups: Hot flushes: No history of carcinoma of the breast. Hot flushes: Treatment for breast carcinoma, not receiving Tamoxifen. Hot flushes: Treatment for breast cancer including Tamoxifen. For all patients, the initial and follow-up assessments included review of hot flush frequency and severity. Patients also completed their own self-assessment rating after follow-up consultations.</td>
<td>The results indicate useful symptomatic benefit for all three groups of patients.</td>
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<td>Colin (2006)</td>
<td>IV</td>
<td>Allergies, especially respiratory allergies, are one of the indications for which homeopathic treatment is most frequently sought. The progress of 147 cases of respiratory allergy since in private homeopathic practice is reported here. Only two cases of ear, nose and throat (ENT) allergies out of a total of 105 showed no improvement, no patients deteriorated. Two cases with worsening and three without improvement were noted out of 42 cases of pulmonary allergies. The constitutional homeopathic remedies varied, Lycopodium, Pulsatilla and Sulphur were most frequently prescribed for ENT allergies, there was no predominantly prescribed remedy in the pulmonary allergy group. Thirty one cases of respiratory allergies consulted only once. The reasons for such a state have been reviewed. If all these cases were therapeutic failures, the success rate of the homeopathic treatment is 87.6%.</td>
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<td>Davidson et al. (1997)</td>
<td>IV</td>
<td>In this trial, 12 subjects suffering from major depression, social phobia or panic disorder, were treated for 7 to 80 weeks with individually prescribed homeopathic remedies and assessed on a clinical global improvement scale (CGIS) or self-rated SCL-90 scale and the Social Phobia Scale (SPS). Subjects were given homeopathic treatment either because they asked for it directly or because conventional treatment had been unsuccessful. Over treatment periods between 8 and 80 weeks, 6 of the 12 patients improved to the degree that their symptom scores reduced by &gt;50% using individualised homeopathy.</td>
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<td>Frenkel and Hermoni (2002)</td>
<td>IV</td>
<td>Effects of Homeopathic Intervention on Medication Consumption in Atopic and Allergic Disorders. Fifty-six percent of patients in this study reduced their use of conventional medication following the homeopathic intervention. Patients who used conventional medications for their allergic disorders reduced their medication expense by an average of 60% in the 3-month period following the homeopathic intervention.</td>
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<td>Gerhard and Wallis (2002)</td>
<td>IV</td>
<td>This prospective observational pilot study investigated the effect of individualized homeopathy on male infertility based on sperm count, hormone values and general health. Forty-five subfertile men were treated with single homeopathic remedies for an average of 10.3 months. The drugs were prescribed on the basis of the overall symptomatic situation. The variables 'sperm density', 'percentage of sperm with good progressive motility' and 'density of sperm with good propulsive motility' improved significantly, especially in cases of oligoasthenozoospermia. The general health of patients improved significantly. The following factors emerged as positive predictors of therapy success: alcohol consumption below 30 g/day, non-smoking, the presence of less than five dental amalgam fillings, and no exposure to noxious substances at the workplace and no previous inflammatory genital diseases. The factors stress, age above 36, high coffee consumption and long duration of unwanted childlessness did not have a negative impact on therapy outcome in this study. The rate of improvement in sperm count through homeopathic therapy is comparable to the improvement achieved by conventional therapy, so that individualized-homeopathic treatment may be considered a useful alternative to conventional treatment of subfertile men. For further investigation, a randomised, therapy-controlled clinical study with parallel group design would be useful (homeopathic therapy vs conventional andrological therapy).</td>
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<td>Gimeno (1991)</td>
<td>IV</td>
<td>Homeopathic treatment of ovarian cysts.</td>
<td>40 cases followed over 9 months. 24/25 improvement in menstrual irregularity; 18/18 improvement of dysmenorrhoea; 18/18 disappearance of pelvic pain; 6/6 improvement of spotting; 10/10 improvement of heavy or prolonged menses; 21/21 improvement of mood changes; 6/6 disappearance of premenstrual migraines; 31/33 other symptom improvement.</td>
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<tr>
<td>Gimeno (1996)</td>
<td>IV</td>
<td>Homoeopathic treatment of HPV infections previously treated by other methods</td>
<td>14 people with recurrent HPV, previously unresponsive to microsurgical procedures, were treated with individualised homeopathy and assessed via cytology prior to treatment, during, and 1 year after commencing treatment. At the final 1 year assessment, 11 of the 14 subjects were declared to be cured.</td>
</tr>
<tr>
<td>Goldstein and Glik</td>
<td>IV</td>
<td>Use of and satisfaction with homeopathy in a patient population</td>
<td>Information was provided by 77 clients from 9 clinics in the Los Angeles area, assessing constitutional homeopathic practice. The study also looked at the characteristics of the people involved in the study. At 4 months after treatment, 71% of clients reported improvement in their health status. This is contrasted with the fact that 80% of all clients enrolled in this survey had had previous orthodox medical treatment for their condition which they had found unsuccessful. The most common presenting complaints involved the respiratory, gastrointestinal and female reproductive systems and most clients were highly educated but had little knowledge of homeopathy prior to their treatment with it.</td>
</tr>
<tr>
<td>Harrison et al. (1993)</td>
<td>IV</td>
<td>Homoeopathic Treatment of Burn Scars.</td>
<td>4 people suffering from hypertrophic scarring subsequent to burns were treated with homeopathic Graphites for 3 months. All 4 subjects were relieved of these symptoms. No controls were used for comparison.</td>
</tr>
<tr>
<td>Itamura (2007)</td>
<td>IV</td>
<td>The effectiveness of individualized homeopathic treatment was measured using the patients' own assessments of seven elements (overall impression, improvement of skin condition, reduction of itchiness, reduction of sleep disturbance, satisfaction in daily life, fulfillment at work and satisfaction in human relations) using a nine-point scale similar to the Glasgow Homeopathic Hospital Outcome Scale (GHHOS).</td>
<td>Six patients reported a score of 4 (complete recovery), 23 patients a score of 3 (75% improvement), 24 patients a score of 2 (50% improvement) and 7 patients a score of 1 (25% improvement). A total of 88.3% of patients reported over 50% improvement. Around one-half the patients with AD and eczema reported greater satisfaction in daily life, greater fulfilment at work and greater satisfaction in human relations. The psychological, physical and psychosomatic symptoms and effects of chronic skin diseases are inextricable. Individualized homeopathic treatment can provoke a good response in patients with chronic skin disease; therefore, the holistic approach used in homeopathy may be a useful strategy alongside conventional treatment.</td>
</tr>
<tr>
<td>Study</td>
<td>LOE</td>
<td>Study Details</td>
<td>Outcomes</td>
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<tr>
<td>Itamura and Hosoya (2003)</td>
<td>IV</td>
<td>The objective of the study was to evaluate the efficacy of homeopathic treatment of intractable atopic dermatitis (IAD). Seventeen IAD patients were given individualized homeopathic treatment in addition to conventional dermatological therapy from 6 months to 2 years and 7 months. Although all of the patients had previously been treated with conventional medicine and various psychological approaches, they had had severe conditions and shown no significant sign of improvement. The efficacy of homeopathic treatment was measured by objective assessments of the skin condition and the patients’ own assessments, using a 9 point scale similar to the Glasgow Homeopathic Outcome Scale, was used.</td>
<td>Over 50% improvement was reported in overall impression and in their skin conditions by all patients, in itchiness by 15 of the patients, in sleep disturbance by 10 out of 13 patients, in satisfaction in daily life by nine out of 12, in fulfilment at work by seven out of 11 and in satisfaction with human relations by 10 out of 14.</td>
</tr>
<tr>
<td>Jack (1993)</td>
<td>IV</td>
<td>How I treat Crohn’s Disease.</td>
<td>Review of 16 consecutive patients. In all but 2 cases the patients claimed they had made a significant improvement.</td>
</tr>
<tr>
<td>Khuda-Bukhsh et al. (2005)</td>
<td>IV</td>
<td>Groundwater arsenic (As) has affected millions of people globally distributed over 20 countries. In parts of West Bengal (India) and Bangladesh alone, over 100 million people are at risk, but supply of As-free water is grossly inadequate. Attempts to remove As by using orthodox medicines have mostly been unsuccessful. A potentized homeopathic remedy, Arsenicum Album-30, was administered to a group of As affected people and thereafter the As contents in their urine and blood were periodically determined. The activities of various toxicity marker enzymes and compounds in the blood, namely aspartate amino transferase, alanine amino transferase, acid phosphatase, alkaline phosphatase, lipid peroxidation and reduced glutathione, were also periodically monitored up to 3 months. The results are highly encouraging and suggest that the drug can alleviate As poisoning in humans.</td>
<td></td>
</tr>
<tr>
<td>Maas (1993)</td>
<td>IV</td>
<td>Ulcerative colitis treated with homoeopathy. A retrospective survey.</td>
<td>Of the 24 cases, 16 had a good outcome, 5 moderate, 3 poor</td>
</tr>
<tr>
<td>Martinez (1990)</td>
<td>IV</td>
<td>Treatment of 32 patients with ‘Folliculinum’, 88% improved over a 2-4mth period.</td>
<td></td>
</tr>
<tr>
<td>Muscari-Tomaioli et al. (2001)</td>
<td>IV</td>
<td>Observational study of quality of life in patients with headache, receiving homoeopathic treatment. 60% of 53 patients with Hx of headache of at least 2 yrs improved on individualised homeopathic treatment over a 4-6mth period.</td>
<td></td>
</tr>
<tr>
<td>Popov (1992)</td>
<td>IV</td>
<td>Homeopathy in treatment of patients with fibromyoma of uterus</td>
<td>Treatment from 1-3yrs of 84 patients. Pain improved in 30 of 38; abnormal endometrial bleeding improved in 30 of 40; significant reduction in tumour volume in 28.6% and increase in volume seen in 19%.</td>
</tr>
<tr>
<td>Reilly et al. (2007)</td>
<td>IV</td>
<td>Outcome related to impact on daily living: preliminary validation of the ORIDL instrument.</td>
<td>70 of 105 patients reported improvements in daily living over 12mths treatment.</td>
</tr>
<tr>
<td>Richardson (2001)</td>
<td>IV</td>
<td>Patient benefit survey: Liverpool Regional Department of Homœopathic Medicine</td>
<td>1100 patients surveyed assessed their improvement: -3(0.09%), -2(1.3%), -1(0.9%), 0(21%), +1(16.3%), +2(27.7%), 3(31.5%), +4(1.1%)</td>
</tr>
<tr>
<td>Study</td>
<td>LOE</td>
<td>Study Details</td>
<td>Outcomes</td>
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<tr>
<td>Robinson (2006)</td>
<td>IV</td>
<td>To assess homeopathic consultations in NHS general practice over a 12-month study period; to analyse the conditions treated homeopathically and assess the responses to homeopathy prescribed in a standard 10 min GP consultation. Data on each homeopathic consultation over 12 months were recorded: including patient details; condition/diagnosis; response score; prescribed medicine; prescribing strategy; medical specialty category. Clinical response was scored using a modified version of the Glasgow Homeopathic Hospital Outcome Scale.</td>
<td>Over the 12-month study period, a total of 5,331 consultations were conducted within the general practice; 489 (9%) of these consultations were homeopathic. A wide variety of conditions were treated homeopathically, 78% of patients had a positive clinical response, 19% no response, 3% negative response. Analysis of the prescribing strategies demonstrated that 73% of the homeopathic prescriptions were issued using the 'problem-based' strategy. The remainder were 'patient-based' (19%), 'context-based' (4%) and 'combined' (4%) strategies. This study illustrates the varied and successful application of homeopathy within the general practice setting. Response scores reveal the beneficial effects of homeopathic treatment. This study supports the use of homeopathy within NHS general practice, delivered in a 10 min consultation.</td>
</tr>
<tr>
<td>Sanchez-Resendiz and Guzman-Gomez (1997)</td>
<td>IV</td>
<td>Polycystic Ovary Syndrome.</td>
<td>Pulsatilla 6C 4th hrly for the 2 weeks for 4 cycles was given to 36 women with oligomenorrhea or amenorrhea, polycystic ovaries on U/S and mental symptoms of Pulsatilla. Complete resolution of all these criteria occurred in 30 women &amp; 4 of the others became asymptomatic.</td>
</tr>
<tr>
<td>Schlappack (2004)</td>
<td>IV</td>
<td>Homeopathic treatment of radiation induced itching in breast cancer patients. A prospective observational study.</td>
<td>25 women suffering from post-radiotherapy induced itching were treated at the University of Vienna's Department of Radiotherapy and Radiobiology using individualised homeopathic medicines. After assessment (1-27 days after beginning the treatment) it was found that homeopathic treatment had been successful in 21 of the women enrolled in the study</td>
</tr>
<tr>
<td>Spence (1991)</td>
<td>IV</td>
<td>Homeopathic treatment of eczema: a retrospective survey of 130 cases.</td>
<td>Review of 130 consecutive patients followed for up to 11yrs. 91% were either better or much better, 7.4% unchanged and 1.6% deteriorated.</td>
</tr>
<tr>
<td>Spence et al. (2005)</td>
<td>IV</td>
<td>Treatment for Chronic Disease: A 6-Year, University-Hospital Outpatient Observational Study</td>
<td>6544 consecutive patients, 70.7% reported positive health changes (50.7% being +2 or +3)</td>
</tr>
<tr>
<td>Steinsbekk and Ludtke (2005)</td>
<td>IV</td>
<td>Patients’ assessments of the effectiveness of homeopathic care in Norway: A prospective observational multi-centre outcome study.</td>
<td>70% of patients reported a meaningful improvement in their main complaint 6 months into treatment. The proportion of patients using conventional medication reduced from 39% to 16%.</td>
</tr>
<tr>
<td>van Erp and Brands (1996)</td>
<td>IV</td>
<td>Homoeopathic treatment of Malaria in Ghana. Open study and clinical trial</td>
<td>90.7% of 75 patients responded to individualised homeopathic treatment, and in an RCT 83% responded to homeopathy compared to 72% who responded to chloroquine.</td>
</tr>
<tr>
<td>van Wassenhoven (1996)</td>
<td>IV</td>
<td>Retrospective study of rheumatological patients in a private homeopathic medical practice.</td>
<td>The 99 'arthritis' patients were reviewed; 43 were able to stop all conventional medication, most failures were in-patients with relatively little follow-up.</td>
</tr>
<tr>
<td>van Wassenhoven (1998)</td>
<td>IV</td>
<td>Retrospective study of cardiac rhythm disorders.</td>
<td>50% of the patients included in this study stopped the use of allopathic drugs; this group included all patients with supraventricular tachycardia.</td>
</tr>
<tr>
<td>Study</td>
<td>LOE</td>
<td>Study Details</td>
<td>Outcomes</td>
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</tr>
<tr>
<td>Vozianov and Simeonova (1990)</td>
<td>IV</td>
<td>Homeopathic treatment of patients with adenomas of the prostate</td>
<td>23/27 patients with nocturia showed reduction in frequency and improved strength of stream; 8/9 patients with urinary urgency improved; 12/15 patients with daytime frequency improved; 19 patients also had chronic prostatitis - 18/19 with perineal, groin and loin pain improved; 17/19 had no exacerbations of prostatitis during the 6-9mths observation, where previously they had used antibiotics (average) every 6-8wks. 13 patients showed subjective improvement in sexual function, none reported worsening. According to radioisotope analysis in 83% residual urine volume was decreased, and in 60% the urofluorometric index improved.. Adenoma size, however, was not demonstrably decreased. Concomitant diseases: diabetes, hypertension, ischaemic heart disease, G.I.T., and skin complaints reduced.</td>
</tr>
<tr>
<td>Witt et al. (2008)</td>
<td>IV</td>
<td>In a prospective, multicentre cohort study with 103 homeopathic primary care practices in Germany and Switzerland, data from all patients (age &gt;1 year) consulting the physician for the first time were observed. The main outcome measures were: The patients’ perceived change in complaint severity (numeric rating scales from 0 = no complaint to 10 = maximal severity) and quality of life as measured by the SF -36 at baseline, and after 2 and 8 years.</td>
<td>A total of 3,709 patients were studied, 73% (2,722 adults, 72.8% female, age at baseline 41.0 ± 12.3; 819 children, 48.4% female, age 6.5 ± 4.0) contributed data to the 8-year follow-up. The most frequent diagnoses were allergic rhinitis and headache in adults, and atopic dermatitis and multiple recurrent infections in children. Disease severity decreased significantly (p &lt; 0.001) between baseline, 2 and 8 years (adults from 6.2 ± 1.7 to 2.9 ± 2.2 and 2.7 ± 2.1; children from 6.1 ± 1.8 to 2.1 ± 2.0 and 1.7 ± 1.9). Physical and mental quality of life scores also increased considerably. Younger age, female gender and more severe disease at baseline were factors predictive of better therapeutic success. Conclusion: Patients who seek homeopathic treatment are likely to improve considerably. These effects persist for as long as 8 years.</td>
</tr>
</tbody>
</table>
## Pre-clinical and veterinary evidence for homoeopathy

### 2.8. Outcomes and level of clinical evidence (LOE) for case series of pre-clinical and veterinary trials

<table>
<thead>
<tr>
<th>Study</th>
<th>LOE</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>Barvalia (2011)</td>
<td>IV</td>
<td>Significant improvement seen in a series of 60 autistic children within 6 mths.</td>
</tr>
<tr>
<td>Bawden (2012)</td>
<td>IV</td>
<td>Six months after the initiation of treatment 155 (84.7%) felt an improvement in their condition with 148 (81%) attributing this to homeopathy. Nobody reported deterioration due to homeopathic treatment; conventional drug use was reduced in 46 patients (25%).</td>
</tr>
<tr>
<td>Bolognani (2011)</td>
<td>IV</td>
<td>High urinary zinc levels was associated with ADHD, and treatment with Zincum met 12C daily was associated with symptomatic improvement as well as reduction in urinary loss.</td>
</tr>
<tr>
<td>Chatterjee et al. (2011)</td>
<td>IV</td>
<td>Psorinum-6x was administered orally to all the participants up to 0.02 ml/Kg body weight as a single dose in empty stomach per day for 2 years along with allopathic and homeopathic supportive cares. 158 participants (42 of stomach, 40 of gall bladder, 44 of pancreatic, 32 of liver) were included in the final analysis of the study. Complete tumor response occurred in 28 (17.72%) cases and partial tumor response occurred in 56 (35.44%) cases. Double-blind randomized controlled clinical trial should be conducted for further scientific exploration of this alternative cancer treatment.</td>
</tr>
<tr>
<td>Danno et al. (2012)</td>
<td>IV</td>
<td>A significant decrease in the frequency, severity, and duration of migraine attacks was observed and, consequently, reduced absenteeism from school.</td>
</tr>
<tr>
<td>Danno et al. (2013)</td>
<td>IV</td>
<td>23 women were treated with individualised homeopathy. The mean decrease in symptom score (7.4) was statistically significant (p &lt; 0.0001). Twenty-one women reported that their QoL also improved significantly (91.3%; p &lt; 0.0001).</td>
</tr>
<tr>
<td>Eizayaga and Eizayaga (2012)</td>
<td>IV</td>
<td>Of 42 eligible patients, 21 had other atopic co-morbidities and 28 (66.7%) were moderate or severe cases. Sixteen (38.1%) patients dropped out. Significant differences were found comparing first and last consultations in mean percentage (95%CI) of affected skin area, 21.1% versus 5.5% respectively (P = 0.002); in the change of the four patients' assessed criteria for atopic dermatitis (P &lt; 0.0001), Itch (P &lt; 0.0001), General wellbeing(P &lt; 0.0188), and Sleep (P &lt; 0.0073). Homeopathic aggravations were reported after 29.8% of prescriptions. Twelve individualized homeopathic medicines were prescribed, Sulphur accounting for 60% of cases with good treatment response.</td>
</tr>
<tr>
<td>Grundling et al. (2012)</td>
<td>IV</td>
<td>The symptoms of patients undergoing homeopathic treatment were shown to improve substantially and conventional medication dosage could be substantially reduced.</td>
</tr>
<tr>
<td>Hati et al. (2012)</td>
<td>IV</td>
<td>85% of patients' symptoms improved despite no reduction in prostate size.</td>
</tr>
<tr>
<td>Jaeger et al. (2008)</td>
<td>IV</td>
<td>In this small pilot study, HIV-patients with suppressive HAART but without immunological response for more than12 months seemed to benefit from a 16 week-treatment with the homeopathic drug combination Canova. After an observation time of nearly 6 months after stopping Canova, we still observed an immunological improvement compared to the pre Canova period.</td>
</tr>
<tr>
<td>Mohan (2007)</td>
<td>IV</td>
<td>81 children treated over 2 yrs with individualised homeopathy. Exacerbations and the use of nebulisers were reduced.</td>
</tr>
<tr>
<td>Nayak et al. (2010)</td>
<td>IV</td>
<td>638 children completed the protocol. 74.4% were cured within 3.9 +/- 1.1 days of treatment.</td>
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<tr>
<td>Study</td>
<td>LOE</td>
<td>Outcomes</td>
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<tr>
<td>Nayak et al. (2012)</td>
<td>IV</td>
<td>550 patients were followed for at least 6 mths. There was a statistically significant reduction in symptoms (P = 0.0001, Friedman test) after 3 and 6 months of treatment</td>
</tr>
<tr>
<td>Ramchandani (2010)</td>
<td>IV</td>
<td>Case series of 30 children &lt; age 5yrs. The number of attacks of the URTIs during the 6 months period preceding the date of commencement of the individualised homeopathic treatment (Control value) and 6 months period following the date of commencement of treatment (Treatment value) were compared indicating statistically significant differences (p&lt;0.001%, t-test and Wilcoxon non-parametric test) in favour of homoeopathic treated cases.</td>
</tr>
<tr>
<td>Rossi et al. (2009)</td>
<td>IV</td>
<td>74% of patients reported at least moderate improvement</td>
</tr>
<tr>
<td>Rossi et al. (2012)</td>
<td>IV</td>
<td>These preliminary results seem to confirm a positive therapeutic effect of homeopathy in atopic children. Furthermore, according to the data from the literature paediatric patients treated with homeopathy seem to show a reduced tendency to maintain AD and develop asthma (and allergic rhinitis) in adult age.</td>
</tr>
<tr>
<td>Shafei et al. (2012)</td>
<td>IV</td>
<td>Severity of asthma improved over 3 and 6 mths in these 30 children</td>
</tr>
<tr>
<td>Witt et al. (2008)</td>
<td>IV</td>
<td>A total of 3,709 patients were studied, the most frequent diagnoses were allergic rhinitis and headache in adults, and atopic dermatitis and multiple recurrent infections in children. Disease severity decreased significantly, physical and mental quality of life sores also increased considerably. Younger age, female gender and more severe disease at baseline were factors predictive of better therapeutic success. Patients who seek homeopathic treatment are likely to improve considerably. These effects persist for as long as 8 years.</td>
</tr>
<tr>
<td>Witt et al. (2009b)</td>
<td>IV</td>
<td>Forty-five physicians treated 82 adults, aged 41.6 +/- 12.2 (mean +/- SD) years. Patients had psoriasis for 14.7 +/- 11.9 years; 96.3% had been treated before. Complaint severity improved markedly over 2 yrs with QOL improvement.</td>
</tr>
<tr>
<td>Witt et al. (2009c)</td>
<td>IV</td>
<td>134 people suffering from sinusitis on average for 10 years and most of these people had had prior treatment for the condition with conventional medicine. The trial participants were monitored every 3 months for 2 years from baseline, and again at 8 years. It was apparent that the homeopathic treatment was associated with improvements in quality of life and a reduction in the complaint severity of sinusitis, which persisted for at least 8 years.</td>
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</table>
### 2.9. Outcomes and level of clinical evidence (LOE) for trials of bacteria, animal and tumour cells

<table>
<thead>
<tr>
<th>Study</th>
<th>LOE</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Endler et al. (2010)</td>
<td>I</td>
<td>A total of 107 studies were found. Of these, 30 were initial studies. In the attempt to reproduce one of these initial studies, 53 follow-up studies yielded comparable effects (35 laboratory-internal, 8 multicenter, 10 independent repetitions), eight studies showed a consistent, yet different result from the initial study (2 laboratory-internal, 2 multicenter, 4 independent repetitions), and 16 studies yielded no effects (5 laboratory-internal, 2 multicenter, 9 independent repetitions). When all repetitive studies are considered, 69% reported effects comparable to that of the initial study, 10% different effects, and 21% no effects.</td>
</tr>
<tr>
<td>Ennis (2010)</td>
<td>I</td>
<td>The methods are poorly standardized between laboratories – although the same is true for conventional studies. Certainly there appears to be some evidence for an effect – albeit small in some cases – with the high dilutions in several different laboratories using the flow cytometric methodologies. After standardization of a number of parameters, it is recommended that a multi-centre trial be performed to hopefully put an end to this “never-ending story”.</td>
</tr>
<tr>
<td>Kuzeff (2012)</td>
<td>I</td>
<td>It was hypothesized that toxicity of a chemical agent could be counteracted by a homeopathic preparation of the enantiomer of the chemical agent. A diverse body of data, including controlled laboratory studies, supports the conclusion that toxicity of optical isomers may be inhibited by homeopathic enantiomer preparations.</td>
</tr>
<tr>
<td>Lingg and Endler (2011)</td>
<td>I</td>
<td>The results of experiments on highland Rana temporaria treated with thyroxine potency 30x are presented in full detail based on this normalisation method. Thyroxine 30x does slow down their metamorphosis. This was observed by 5 researchers in 20 sub-experiments, and it seems to be the most reliable bio-assay found in amphibian research on homeopathy so far.</td>
</tr>
<tr>
<td>Sainte-Laudy and Belon (2009)</td>
<td>I</td>
<td>The main results obtained over 28 years of work was the demonstration of a reproducible inhibition of human basophil activation by high dilutions of histamine, the effect peaks in the range of 15–17CH. The effect was not significant when histamine was replaced by histidine (a histamine precursor) or cimetidine (histamine H2 receptor antagonist) was added to the incubation medium. These results were confirmed by flow cytometry. Using the mouse model, we showed that histamine high dilutions, in the same range of dilutions, inhibited histamine release.</td>
</tr>
<tr>
<td>Banerjee et al. (2010b)</td>
<td>II</td>
<td>Both potencies of Chel exhibited anti-tumor and anti-oxidative stress potential against artificially induced hepatic tumors and hepatotoxicity in rats.</td>
</tr>
<tr>
<td>Bellavite et al. (2011)</td>
<td>II</td>
<td>Gelsemium. sempervires 5,7, &amp; 30C influenced the emotional responses of mice to novel environments, suggesting an improvement in exploratory behavior and a diminution of thigmotaxis or neophobia.</td>
</tr>
<tr>
<td>Bellavite et al. (2012)</td>
<td>II</td>
<td>Up to 14 separate replications were carried out in fully blind and randomised conditions. Pooled analysis demonstrated highly significant effects of Gelsemium s. 5C, 7C, and 30C, confirming the evidence that Gelsemium s. regulates emotional responses and behaviour of laboratory mice in a nonlinear fashion with dilution/dynamization.</td>
</tr>
<tr>
<td>Berchieri et al. (2006)</td>
<td>II</td>
<td>180 chickens were divided into 4 groups. 2 of these groups were given pre-treatment with placebo and 2 were given different pre-treatment with preparations of a homeopathic nosode made from an antibiotic resistant strain of Salmonella enterica (Enteritidis) at a 30X potency, over a 10 day period. On day 17 the chickens were challenged with a culture of the same species of Salmonella from which the nosode was made. Cloacal swabs taken twice daily from the chickens at this point revealed that the birds that received the nosode showed a significant reduction in the growth of the bacteria compared to those given placebo.</td>
</tr>
<tr>
<td>Bhattacharjee et al. (2009)</td>
<td>II</td>
<td>Administration of Nat Sulph 200 reduced genomic damage, activities of AcP, AlkP, AST, ALT, LPO and increased GSH content.</td>
</tr>
<tr>
<td>Biswas and Khuda-Bukhsh (2004)</td>
<td>II</td>
<td>Chelidonium 30 and 200 provided a significant protection against the carcinogens, and favourably modulated some of the haematological markers normally associated with hepatotoxicity.</td>
</tr>
</tbody>
</table>
Biswas et al. (2005) II Both Carcinosin 200 and Chelidonium 200 when administered alone show considerable ameliorative effect against p-DAB-induced hepatocarcinogenesis in mice; but the conjoint feeding of these two drugs appears to have had a slightly greater protective effect.

Bonamin et al. (2012) II F1 rats born to dexamethasone 15 cH treated females presented significant increase in mast cell degranulation, decrease in monocyte percentage, increase in CD18+ PMN cells, and early expression of ED2 protein, in relation to control. The results show that the exposure of parental generation to highly diluted dexamethasone interferes in inflammation modulation in the F1 generation.

Camerlink et al. (2010) II E Coli 30C reduces E coli diarrhoea to a significant extent.

de Oliveira et al. (2011) II The results allow us to conclude that highly diluted to the 200C Merc sol modulates reactive oxygen species (ROS), reactive nitrogen species (RNS) and cytokine secretion, which are central mediators of the immune system, wound healing and body homeostasis.

Giesel et al. (2012) II Belladonna 30C and ant 30C significantly reduce the daily foraging activity of ants.

Guajardo-Bernal et al. (1996) II In a blind, placebo-controlled trial, Sulphur 201C was given to pregnant sows every 10 days, and extending into the feeding period after birth. By day 30 the piglets fed by the sows given the velum exhibited a higher final weight, mean total and daily weight gain, indicating that not only was the remedy effective, but that its effects were transmitted through the sows’ milk.

Haine et al. (2012) II Dilutions 12cH and 30cH of Acon exhibited anxiolytic effects on the CNS in an animal experimental model.

Hielm-Bjorkman et al. (2009) II Our results indicated that the HCP Zeel® ad us. vet. was beneficial in alleviating chronic orthopedic pain in dogs although it was not as effective as carprofen.

Lakshmipathy Prabhu et al. (2012) II Both diazepam and Puls showed significant anxiolytic activity compared to control. The anxiolytic effect is greater for the 3x dilution than 6x dilution of Puls

Mohammadi et al. (2012) II Hypericum 30C significantly improved nerve regeneration.

Neumann et al. (2011) II Clinical signs of OA improved significantly to the end of the 56 day treatment period, effectiveness was comparable in both groups. Both treatment regimens were well tolerated with only three treatment-related adverse events, all in the carprofen group.

Patel et al. (2012) II The 1M, 10M and CM homeopathic dilutions of Rhus tox reduced primary and secondary arthritic lesions, improved body weight gain and protected rats against CFA-induced hematological and radiological perturbations. A significant reduction in the serum levels of CRP and an improvement in pain threshold of injected paws was observed in the groups treated with the Rhus tox dilutions.

Patil et al. (2011) II The 1M, 10M and CM homeopathic dilutions of Rhus tox reduced primary and secondary arthritic lesions, improved body weight gain and protected rats against CFA-induced hematological and radiological perturbations. A significant reduction in the serum levels of CRP and an improvement in pain threshold of injected paws was observed in the groups treated with the Rhus tox dilutions.

Piau et al. (2012) II 4800 post-larval fish treated with the homeopathic complex had improved survival and muscle fiber hypertrophy, but were smaller (probably related to increased survival and overcrowding) compared to fingerlings treated with synthetic hormone or control.

Sato et al. (2012) II The thymulin 5cH treated group had increased productivity index compared to control (391.45 versus 261.93) associated with higher viability in the 7th week (p = 0.013).

Spin-Neto et al. (2010) II Both removal torque and radiographic bone density evaluation showed that Symphyum. officinale 6cH enhanced bone formation around the micro-implants, mainly at 14 days. At 56 days, the radiographic bone density was higher in the treated group.
<table>
<thead>
<tr>
<th>Study</th>
<th>LOE</th>
<th>Outcomes</th>
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<tr>
<td>Sukul et al. (2001)</td>
<td>II</td>
<td>Potentially alcoholic laboratory rats, after being divided into 4 groups, were given a choice of drinking from bottles containing either 20% ethanol in water or plain water. The rats were given diluent, or strychnine, or Nux vomica tincture, or Nux vomica 30C. When compared to the control group (diluent only) both the Nux vomica tincture and Nux vomica 30C groups of rats showed a distinct aversion to the 20% ethanol drinking bottle.</td>
</tr>
<tr>
<td>Datta et al. (1999)</td>
<td>III-I</td>
<td>The combined pre- and post-feeding of Arsenicum album was found to be most effective in reducing the genotoxic effects of As2O3 i200C was more effective than 30C.</td>
</tr>
<tr>
<td>Datta et al. (2001)</td>
<td>III-I</td>
<td>Both Cad Sulph-30 and 200 were able to combat cadmium induced genotoxic effects in mice and that combined pre- and post-feeding mode of administration was found to be most effective in reducing the genotoxic effect of CdCl2 followed by the post-feeding mode.</td>
</tr>
<tr>
<td>Frenkel et al. (2010)</td>
<td>III-I</td>
<td>The ultra-diluted Carcinosin, Phytolacca, Conium and Thuja exerted preferential cytotoxic effects against the two breast cancer cell lines, causing cell cycle delay/arrest and apoptosis. This was accompanied by altered expression of the cell cycle regulatory proteins, including downregulation of phosphorylated Rb and upregulation of the CDK inhibitor p27.</td>
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<tr>
<td>Guimarães et al. (2009)</td>
<td>III-I</td>
<td>Co-culture of macrophages with lymphocytes in the presence of the CHM enhanced the anti-cancer performance of lymphocytes against a very aggressive lineage of melanoma cells. These results suggest that non-toxic therapies using CHMs are a promising alternative approach to the treatment of melanomas. In addition, they are attractive combination-therapy candidates, which may enhance the efficacy of conventional medicines by improving the immune response against tumor cells.</td>
</tr>
<tr>
<td>Lotfollahzadeh et al. (2012)</td>
<td>III-I</td>
<td>Rectal temperature, healing of inflamed mucosal areas and appetite score all demonstrated significant therapeutic effect.</td>
</tr>
<tr>
<td>Sukul et al. (2005)</td>
<td>III-I</td>
<td>Mice infected with Trichinella spiralis were given Podophyllum as a homeopathic mother tincture, Cina 30C, Santonin 30C, ethanol 30C, and an untreated control group. After 120 days the mice were examined for the presence of the T. spiralis larvae in muscle. At 120 days the mice given Podophyllum had their larval load reduced by 61% when compared to the control, those given Santonin had a reduction of 81% and the mice given Cina had a reduction of 84%.</td>
</tr>
<tr>
<td>Bagai et al. (2012)</td>
<td>III-2</td>
<td>Nosode 30 possesses considerable in vivo antiplasmodial activity against P. berghei infection as compared to Nosode 200 as evident from the chemosuppression obtained using Peter's 4-day test. Further studies on the drug can be carried out to establish its antimalarial potential in monotherapy or in combination with other homeopathic drug formulations.</td>
</tr>
<tr>
<td>Bandyopadhyay et al. (2010)</td>
<td>III-2</td>
<td>Ultradiluted belladonna could inhibit JE virus infection</td>
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<tr>
<td>Chandrakant and Varshney (2007)</td>
<td>III-2</td>
<td>These results reveal broad activity of B. orientalis MT. It may have nonselective anti-asthmatic activity. The anti-anaphylactic activity of B. orientalis MT may be due to mast cell stabilization, suppression of IgE and eosinophil cell count.</td>
</tr>
<tr>
<td>Chaudhuri and Varshney (2007)</td>
<td>III-2</td>
<td>Infestation by Babesia gibsoni is a protozoa normally transmitted by ticks. Treatment of 13 dogs with Crotalus horridus 200C was compared with that of 20 dogs with standard treatment diminazine aceturate. At 18 days after the medications were given, it was found that Crotalus horridus 200C provided the same level of clinical recovery.</td>
</tr>
<tr>
<td>de Camargo et al. (2013)</td>
<td>III-2</td>
<td>When administrated orally, Arnica 30cH protects against hepatic mitochondrial membrane permeabilization induced by Ca(2+) and/or Fe(2+)-citrate-mediated lipid peroxidation and fragmentation of proteins due to the attack by reactive oxygen species.</td>
</tr>
<tr>
<td>dos Santos et al. (2007)</td>
<td>III-2</td>
<td>We found significant reductions compared to control in carrageenan-induced paw oedema, vascular permeability, writhing induced by intraperitoneal acetic acid and stress induced gastric lesions.</td>
</tr>
<tr>
<td>Eizayaga et al. (2005)</td>
<td>III-2</td>
<td>Aspirin 14C had a measurable prothrombotic effect compared to controls.</td>
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<td>Glatthaar-Saalmuller (2007)</td>
<td>III-2</td>
<td>Control substances were acyclovir (10 μg/mL), ribavirin (6 μg/mL), and amantadine hydrochloride (5 μg/mL), depending on the virus type. Gripp-Heel demonstrated dose-dependent in vitro activity (significant reductions of infectivity by 20% to 40%) against Human herpes virus 1, Human adenovirus C serotype 5, Influenza A virus, Human respiratory syncytial virus, Human parainfluenza virus 3, Human rhinovirus B serotype 14, and Human coxsackievirus serotype A9.</td>
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<tr>
<td>Harrer (2013)</td>
<td>III-2</td>
<td>In the author’s own experiment, there was a clear trend of Thyroxine 30x animals developing more slowly than placebo animals, which is in line with the previous experiments. In the analysis of all available data with regard to the 4-legged stage, pooled T30x values from the initial team were 10.1% smaller than placebo (100%) and pooled T30x values from the 5 independent researchers were 12.4% smaller (p &lt; 0.01 and d &gt; 0.08). Analogously, the number of animals entering the juvenile stage with reduced tail was smaller for T30x than placebo.</td>
</tr>
<tr>
<td>Hofbauer et al. (2010)</td>
<td>III-2</td>
<td>Strychnos Nux vomica (Nux vomica) and Calendula officinalis are used in highly diluted form in homeopathic medicine to treat patients suffering from gastritis and gastric ulcers. Addition of Nux vomica 10c and Calendula officinalis 10c in a 43% ethanolic solution led to a significant reduction of H. pylori induced increase in gene expression of HB-EGF (reduced to 53.12+/−0.95% and 75.32+/−1.16% vs. control; p&lt;0.05), respectively. Nux vomica 12c reduced HB-EGF gene expression even in dilutions beyond Avogadro’s number (55.77+/−1.09%; p&lt;0.05). Nux vomica 12c in a 21.5% ethanol showed a smaller effect (71.80+/−3.91%, p&lt;0.05).</td>
</tr>
<tr>
<td>Khuda-Bukhsh et al. (2011b)</td>
<td>III-2</td>
<td>Thujone-rich Fraction showed and matched all the anti-cancer responses of Thuja occidentalis mother tincture (TOΦ) and could be the main bio-active fraction. The use of TOΦ in traditional medicines against tumors has, therefore, a scientific basis.</td>
</tr>
<tr>
<td>Kumar et al. (2007)</td>
<td>III-2</td>
<td>These studies with rats and mice demonstrate that homeopathic drugs, at ultra low doses, may be able to decrease tumor induction by carcinogen administration.</td>
</tr>
<tr>
<td>Oryan (2012)</td>
<td>III-2</td>
<td>Treatment reduced signs of acute inflammation and strongly ameliorated clinical symptoms, structural organization and biomechanical properties (p &lt; 0.05). Apparently, TC is effective in restoring the clinical, morphological and biomechanical properties of the injured SDFT in rabbits and may be valuable in human and veterinary medicine.</td>
</tr>
<tr>
<td>Pathak et al. (2003)</td>
<td>III-2</td>
<td>Fifteen patients diagnosed with intracranial tumors were treated with Ruta 6C and Ca3(PO4)2 3x. 7 of these had glioma, 6 of which regressed completely. Human brain cancer and HL-60 leukemia cells, normal B-lymphoid cells, and murine melanoma cells were treated in vitro with different concentrations of Ruta in combination with Ca3(PO4)2. Cancer cell death was initiated by telomere erosion and completed through mitotic catastrophe events. Conclusion; Ruta 6C in combination with Ca3(PO4)2 could be used for effective treatment of brain cancers, particularly glioma.</td>
</tr>
<tr>
<td>Pathak et al. (2006)</td>
<td>III-2</td>
<td>Lycopodium 30 provided protection against the effects of the carcinogen</td>
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<tr>
<td>Ruiz-Vega et al. (2003)</td>
<td>III-2</td>
<td>In this blinded and controlled study, rats were given caffeine and then Coffea 30C in an effort to determine what effects, if any, the Coffea 30C had on sleep characteristics. The homeopathic remedy was found to increase the intensity of sleep in the rats when compared with the effects of the control used.</td>
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<tr>
<td>Siguiera et al. (2013)</td>
<td>III-2</td>
<td>Influenzinum RC did not cause cytotoxic effects but induced morphological alterations in Madin–Darby canine kidney (MDCK) cells. After 30 days, a significant increase (p &lt; 0.05) in mitosis rate was detected compared to control. MDCK mitochondrial activity was changed after treatment for 10 and 30 days. Treatment significantly diminished (p &lt; 0.05) PFK-1 activity. TNF-α in biotherapy-stimulated J774.G8 macrophages indicated a significant (p &lt; 0.05) increase in this cytokine when the cell supernatant was analyzed.</td>
</tr>
<tr>
<td>Silva et al. (2008)</td>
<td>III-2</td>
<td>Significant difference in tick numbers between cattle treated with homeopathic mix of parasites and controls.</td>
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<tr>
<td>Soto et al. (2008)</td>
<td>III-2</td>
<td>Piglets of the homeopathic treated group had significantly less E. coli diarrhoea than piglets in the placebo group (P&lt;0.0001). Especially piglets from first parity sows gave a good response to treatment with Coli 30C. The diarrhoea seemed to be less severe in the homeopathically treated litters, there was less transmission and duration appeared shorter.</td>
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<tr>
<td>Study</td>
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<td>Outcomes</td>
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<td>Sunila et al. (2007)</td>
<td>III-2</td>
<td>Ruta 200C and Hydrastis 200C and 1M and Thuja 1M are shown to have significant antitumour activity.</td>
</tr>
<tr>
<td>Tavares Carvalho et al. (2009)</td>
<td>III-2</td>
<td>Homeopathic complex Tepeex® is a compound of Actaea racemosa 4cH, Natrum muriaticum 2cH, Pulsatilla nigricans 3cH, Chamomilla 3cH and Sepia succus 5cH. Male Wistar rats demonstrated that the homeopathic complex Tepeex® has anxiolytic and antidepressant properties without affecting motor coordination.</td>
</tr>
<tr>
<td>Varshney and Naresh (2005)</td>
<td>III-2</td>
<td>The effectiveness of homeopathic complex in the treatment of acute non-fibrosed mastitis was 86.6% with a mean recovery period of 7.7 days (range 3–28), and total cost of therapy as Indian Rupees 21.4. The corresponding cure rate for the antibiotic group was 59.2% with a mean recovery period of 4.5 days (range 2–15) and an average treatment cost of Rs.149.20. We conclude that the combination of Phytolacca, Calcarea fluorica, Silica, Belladonna, Bryonia, Arnica, Conium and Ipecacuanha (Healwell VT-6) was effective and economical in the management of mastitis in lactating dairy cows.</td>
</tr>
<tr>
<td>de Souza et al. (2012)</td>
<td>IV</td>
<td>The use of homeopathy apparently improved the production of viable doses of semen from bulls with previous freezing problems and poor semen quality. Controlled studies should be conducted.</td>
</tr>
<tr>
<td>Garibaldi et al. (2009)</td>
<td>IV</td>
<td>We found that oral administration of low doses IL-12 plus IFN-gamma is able to solve the bronchial hyperresponsiveness condition of mice, establishing normal cytokine levels. The anti-asthma activity was confirmed by histological analysis of lungs and broncho-alveolar lavage fluid cell count. Serum ovalbumin-specific IgE was also significantly inhibited by treatment with low dose activated cytokines solution. These findings may suggest a novel approach to diseases which involve a Th1/Th2 imbalance.</td>
</tr>
<tr>
<td>Mathie and Farrer (2007)</td>
<td>IV</td>
<td>Of 767 individual animals treated (547 dogs, 155 cats, 50 horses, 5 rabbits, 4 guinea-pigs, 2 birds, 2 goats, 1 cow and 1 tortoise), outcomes were obtained in 539 cases: 79.8% showing improvement, 6.1% deterioration, 11.7% no change; outcome not recorded in 2.4% of follow-ups. Strongly positive outcomes (scores of +2 or +3) were achieved in: arthritis and epilepsy in dogs and, in smaller numbers, in atopic dermatitis, gingivitis and hyperthyroidism in cats.</td>
</tr>
<tr>
<td>Mathie et al. (2010)</td>
<td>IV</td>
<td>Outcomes were obtained in 961 cases (75.9% positive, 4.6% negative, 14.7% no change; 4.8% outcome not recorded). Strongly positive outcomes (scores of +2 or +3) were achieved most notably in the frequently treated conditions of anxiety, depression, and irritable bowel syndrome.</td>
</tr>
<tr>
<td>Varshney (2007)</td>
<td>IV</td>
<td>10 dogs with idiopathic epilepsy were given Belladonna 200C during the seizure phase orally at 15min intervals until the seizure activity was reduced, and this was continued then four times daily. Four dogs with head shaking syndrome in addition to seizures were given an additional Cocculus 6C, 3-4 drops orally weekly for 3 months. As a result of this therapy, the numbers of fits reduced to 2-3 during first 2 weeks post-therapy and then became occasional in next 2 weeks. With continuation of Belladonna therapy, no fits were observed during 2-7 months follow-up. In two cases seizures reappeared within 15-25 days of cessation of therapy. Belladonna therapy was resumed and seizure control was again achieved. Owners were advised to continue the therapy at least twice daily until no fits occurred for at least 2 months.</td>
</tr>
</tbody>
</table>
References


significant component of nonallergic rhinitis. *Annals of Allergy, Asthma and Immunology*; 107(2): 171-178.


comparing individualised homeopathic care and waiting-list controls. Complementary Therapies in Medicine; 13(4): 231-238.


Appendix 3
Dear Prof Anderson, Dr Hacker and members of the AHEC,

I understand that your ‘DRAFT NHMRC Public Statement on Homeopathy’ came unintended by yourselves into my email. I read it with surprise, because it suggests your organisation could be better informed in this matter. I discussed the matter with a member of your staff, who said you had no intention of discussing it with representatives or experts in the homeopathic profession. I wonder if you have given adequate consideration to the reliability of the conclusions of the UK House of Commons Science and Technology Committee’s (CSTC) Evidence Check of Homeopathy (1). Your document provides no suggestion that the NHMRC is basing its position on its own investigation, which would be a sad state of affairs for Australia’s peak medical research body, and could be construed as harking back to a British colonial approach to business. This letter is intended to provide you with some perspective, coming from a group of doctors who use Homeopathy in practice.

There are a number of reasons why the CSTC conclusion (that Homeopathy’s clinical effects are no more than placebo effects) is unjustified:

a) Science is not based on what people believe is possible or not possible, rather it relies on data and its appropriate analysis. Meta-analyses are at the top of the pecking order of clinical evidence. They deserve this status only when certain criteria are fulfilled. Systematic reviews may be done with or without meta-analysis, depending on whether the investigator has adequate information to do a formal analysis. Something is not rigorous evidence just because it is called a meta-analysis or systematic review. The ideal meta-analysis is one that is designed prior to the prospective studies (on which it is based) being performed. When meta-analysis is performed retrospectively, it needs to be based on identical studies, or at the very least on very similarly designed studies with similar end points. This necessity is based in statistical theory. The more disparate the studies are, the more assumptions must be made about how to do the analysis; the more speculative the results of the analysis or review becomes. A poor quality meta-analysis can come to diametrically opposite conclusions with minor changes in assumptions, and therefore provides unreliable evidence. Homeopathy comprises many different practices, and the studies collected in reviews to date comprise many different methods and experimental designs. The best quality evidence available at the moment is in the positive statistical association demonstrated by various double-blind randomized controlled trials or blinded randomized controlled laboratory studies. There is no data which demonstrates that homeopathic medicines in general are inactive, although there are specific studies that failed to show efficacy of certain remedies under certain conditions. The studies which have been clumped together in reviews and meta-analyses retrospectively to date are inferior evidence, and lack the homogeneity
to be used for negation of the evidence of positive RCTs and clinical/laboratory studies. (2)

b) Para 69 describes that the CSTC was most influenced by Shang et al's (3) conclusion. Unfortunately, while these authors purported to be designing a review methodology to eliminate publication bias from skewing analyses of homeopathy RCTs, they introduced their own bias into their analysis. "Professor Eggers stated at the onset that he expected to find that homeopathy had no effect other than that of placebo." (4). The CSTC failed to note the unrefuted criticisms of this trial (5,6), which were presented to them in evidence. Quality was assessed differently from previous analyses, and the only conclusion that can be drawn, relating to their predefined hypotheses, is that for the trials chosen, quality of homeopathic trials is better than for conventional trials. The subgroup of homeopathy trials used for the final analysis was not comparable with the group of conventional trials: cut-off values for larger trials differed between the homeopathy and conventional group and Shang's conclusion was based on 8 trials on 8 different indications, which were also not matched with the conventional trials. The result was highly dependent on the cut off point for defining 'larger trials', as well as their subjective decisions about what constituted higher quality, and they did not include a sensitivity analysis to justify the validity of the choices they made in constructing their analysis. Shang also excluded some homeopathy trials because he could not find a matching conventional trial eg Wiesenauer's trial on polyarthritis (7) is a larger trial that could have altered their results. Shang also chose to disregard safety, including trials on some conventional treatments that are no longer available because of serious adverse events. Shang's negative results were largely due to one trial on preventing muscle soreness in 400 long-distance runners, a controversial prophylactic use of the remedy, not usual in clinical practice. In fact 5 other of the 8 large trials used in the final analysis gave the same homeopathic medicine to every subject, regardless of their individual symptoms. Only in unusual circumstances would homeopaths be likely to use these remedies in these clinical situations, one of which was the use of Thyroidinum (a remedy made from thyroid tissue) to induce weight loss. To make valid conclusions about homeopathic practice, one needs to use research that can validly be generalized to clinical practice. Shang ignored this necessity. Consequently Shang's conclusions were not supported by the data, only by his group's biased interpretation of it. One has to ask how the study ever made it through the Lancet's editorial board, also because some of the crucial information (on which some of the criticisms are based) was not included in the publication, eg which 8 trials were used for the analysis! It took 6 months for Shang et al to release this information, time enough for their intended media damage to be achieved. (6 yrs later those 6mths are still having their repercussions!) Considering also that publication's rejection of Ludtke & Rutten's subsequent critique, which is greater, Shang's sham, or the Lancet's shame?

c) In their rush to reach a conclusion, the CSTC failed to consider at least 11 RCTs (noted in the written submissions), which were published subsequent to all the trials considered by Shang et al. Eg one of which (8) shows highly significant results in favour of giving certain intubated patients in ICU a homeopathic remedy based on Potassium bichromate, resulting in a reduction of length of stay by an average of 3 days. This could translate into saving $1000s/patient, and increasing bed availability.
d) The CSTC claimed to be considering the evidence that homeopathic preparations were not placebos, yet completely ignored written evidence submitted by Dr Peter Fisher (HO21) concerning laboratory experiments demonstrating activity in ultradilutions in contexts where the placebo effect is unlikely to be a confusing factor.

e) It appears that the CSTC had the characteristics of a kangaroo court, dancing to 'Sense about Science's' tune. Supporting this conclusion are the fact that they gave contributors a mere 17 days to prepare and submit their evidence, and 60 written submissions and 2 days of hearings were collected by the end of Nov2009. From then to 8th Feb 2010 the CSTC constructed their report of 275 pages, which includes reference to hundreds of scientific articles. One wonders how a group of politicians could do justice to that volume of unfamiliar material in that time frame. The limited breadth of their enquiry (HO46), a - d above, and the analysis of the committee's membership and voting patterns(9) support this conclusion. The report was 'ratified by 3 MPs: 2 of whom were not present at the committee meetings - and one of the two was not even a member of the committee when the hearings were held' and the third has an open history of his predjudice against homeopathy. 1 member was opposed, and a fifth abstained. The other 9 members of the CSTC were not present and provided no indication of their position.

f) Although the CSTC can be excused for not considering trials published after their data collection period, you can not be so excused. In one journal (Homeopathy) I note 5 original research articles which provide evidence against your proposed conclusion (10-14). That is just the first source I have looked at.

g) A consultation aiming at prescribing homeopathy goes beyond collecting the information required to diagnose the pathology (mental or physical), attempting to understand why the patient has become ill, and what is peculiar to this individual in the disease. This information assists in finding the appropriate remedy, but it also takes the patient on a reflective journey, which may add to the healing potential. It may be difficult to be sure whether the consultation, or the remedy taken, initiates the healing process. Most RCTs have compared the homeopathic remedy with a placebo, and there has been little investigation aimed at comparing the consultation's therapeutic potential with standard medical consultations. Trials that fail to investigate this may fail to detect treatment success. Indeed the CSTC makes the point: 'Homeopathic consultations may therefore have a positive impact on patients' perception of the intervention and result in a more powerful placebo effect.' (15) The report goes on to ignore the utility of this benefit, (and the lack of research into it) as if to say that patients should be denied this healing potential because it is unethical as a placebo effect. Should we not be trying to maximise the healing effect of our interaction with our patients, improving our 'bedside manner'?

NOTE that the UK Parliament chose NOT to act on the recommendations of the CSTC. That body felt that it was important to preserve the right of an informed patient to choose their own treatment.
effectiveness of Homeopathy in clinical practice, and the cost effectiveness compared to standard treatment(16). The CSTC ignored all of this, because they said it was outside the remit of the ethical issue they were focussed upon. You appear to be following their lead. However, government and private health insurers would do well to examine it closely, because the companies behind the skeptics and detractors of Homeopathy are aiming to remove marketplace competition, so they can sell more drugs. One wonders why Homeopathy's detractors are so concerned about the 0.004% of the UK NHS budget that Homeopathy consumes, when there are much larger pickings to be found in other areas of modern medicine, eg minimising iatrogenic disease (the third largest killer in the USA). Perhaps to keep the regulators occupied with the small fry, while business continues as usual. Maybe they're disturbed by an inaccessible growing market of patients who use Homeopathy. Maybe they have a variant of OCD which directs them to attempt to stamp out what they can't understand. Or perhaps it is because they have been spooked by the placebo effect itself, which seems to be growing, making it harder to get drugs to market (17).

Much of general medical therapeutics in use today also lacks an evidence base according to the BMJ (18). 'Of around 2500 treatments covered 13% are rated as beneficial, 23% likely to be beneficial, 8% as trade off between benefits and harms, 6% unlikely to be beneficial, 4% likely to be ineffective or harmful, and 46%, the largest proportion, as unknown effectiveness'. Why single out Homeopathy, when it has a stronger evidence base than 50% of those treatments?

Let us change focus from the rarefied world of statistics and clinical trials, to the space involving the patient and clinician. Using homeopathy, we have all experienced clinical situations where a patient with acute illness has responded well, or their warts have disappeared within a week, or a chronic illness the patient has struggled with for years has settled down. I have occasionally seen homeopathy reverse pathology, that I did not expect to be possible eg osteomyelitic bone loss, or neurodegenerative disease. We know that this isn't necessarily the action of the remedies, it could be spontaneous remission, or it could be the effect of the interpersonal relationship (which presumably is somehow more potent than that of the other doctors previously consulted). We are aware that 10% of the Indian health system functions with homeopathy, including hospital medicine. That's around 100 million people in India alone, who make use of Homeopathy: and it's not just the poor and perhaps less educated, it is used throughout the society. The WHO considers Homeopathy to be the second most internationally used medical discipline. It is a relatively safe and cheap system of therapeutics, which adds to its attractiveness. Adding homeopathy to a medical practice is certainly challenging, but for many reasons is interesting and enjoyable. As GPs, our members can attest eg that our use of homeopathic remedies reduces our reliance on antibiotics (and other drugs), assisting the effort to contain the spread of resistant bacterial strains, and diminishing some govt expense through the MBS. For most of us, it has been our experiences rather than clinical trial results that have led to our use of Homeopathy. We applaud those with the perseverance to conduct clinical trials, but our knowledge of the effectiveness of Homeopathy does not rest there. We understand that it is an individual case phenomenon. One cannot guarantee results. One has to work with the healing potential of the patient, and it is an art as well as a science. This is the background to the frame of mind with which the homeopath generally approaches a consultation. There are a few variables that together create the scenarios relevant to the question - Is it ethical to practice homeopathy in this case?
Following are examples:
   a) Patient wants to be managed homeopathically because of good prior experience, or
      referred by another patient/wants 'natural' treatment/ doesn't care what treatment, but
      has heard we can help him/wants some treatment that has been proven to work......
   b) After taking the case I assess Homeopathy has a good/moderate/poor chance of
      helping
   c) There are several other therapeutic options which have/have not been already tried,
      and they have significant/insignificant side effect risk and are financially
      possible/difficult/impossible.

As clinicians we make decisions with every patient concerning whether or not to use
Homeopathy. I hope it has become evident that this does not resolve itself with a universal
answer from a distant bureaucrat; it requires individualisation, and our patients appear to
understand that, indeed they sometimes express their appreciation of it.

Concerning the placebo response. There are people who are healers, who use their
consciousness and 'energy', possibly through their hands, to induce healing. They are
sometimes referred to as 'faith' healers. Are the 'faithful' responding via a placebo effect (ie
their faith in the treatment) and if so, is this therefore unethical practice? The consultation is
an essential part of the process of connecting the remedy to the patient, if it contributes to
the healing power of the remedy, what part of this process is unethical? So long as the patient
and clinician accept that there is a degree of unknown about this process, and the clinician is
not willfully misleading the patient for the clinician's benefit, we are satisfied that we are
behaving ethically.

Your proposed response indicates a lack of independent enquiry and thought, accepting
other's conclusions with a minimum of critical examination, about a subject of which you
appear to have little experience. To come out with a public statement on this basis, degrades
the good name of the NHMRC into nothing more than a common news service. I urge you
therefore to abandon the proposed Statement. If you decide to develop your understanding in
this area, you could start with the Memorandum submitted by the Complementary Medicine
Research Group, University of York (19) and the BHA's response to the CSTC (20), both of
which provide some balance to the CSTC's conclusion and recommendations. You could also
discuss the matter with experts in the field of Homeopathy. Indeed it is worth considering the
ethics of releasing a statement of the nature you are considering, without such consultation.
As well you could extend to Homeopathy your usual business of assisting further research.

Yours sincerely,

Dr Nick Goodman


2. My thanks to Dr Michael Kuzeff for the basis to this paragraph (a).

effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of


http://chestjournal.chestpubs.org/content/127/3/936.full.html


15. CSTC Page 22 Para 81 c)

16. CSTC evidence HO 04, 09,15, 22, 23, 27, 29, 35, 48


18. http://clinicalevidence.bmj.com/ceweb/about/knowledge.jsp
