



An exploration of the relationship between placebo and homeopathy and the implications for clinical trial design

Claire Haresnape

Barts and the London School of Medicine and Dentistry, Queen Mary University of London, William Harvey Research Institute, London, EC1M 6BQ, UK

Correspondence to: Claire Haresnape. Email: C.Haresnape@qmul.ac.uk

DECLARATIONS

Competing interests

This article has been funded by a grant from Biological Heilmittel Heel GmbH and the author has worked on a consultancy basis for BioPathica Ltd, Ashford, Kent

Funding

This work was supported by an educational grant from Biologische Heilmittel Heel GmbH, Dr.-Reckeweg-Str. 2-4,76532 Baden-Baden, Deutschland

Ethical approval

Not applicable

Guarantor

CH

Contributorship

Sole authorship

Summary

Placebo appears to be a real neurobiological phenomenon that has evolved through the selection pressure to be able to heal ourselves. The complex language and social structures of humans means that we can attribute meaning to therapeutic encounters with culturally sanctioned authority figures and we can use our attachment to such figures to generate hope for recovery. Different mechanisms may be involved in the neurobiological aspect of placebo including anxiety, learning, conditioning as well as individual genetic variation. Examination of the published work shows that while some trials do seem to indicate a specific mode of action for homeopathic remedies other trials do not and this is an issue that needs to be addressed at the trial design stage. A clinical trial that includes both a placebo group and a non-participating control arm is the most powerful design for separating the non-specific and polymorphic placebo effect from the specific effects of trial medication. The control variables in a trial of homeopathic medication should also include the process of consultation as this may assume a meaning for the individual that can also be associated with a placebo effect.

Introduction

It is a commonly held belief that homeopathy is 'nothing more' than a placebo effect, a turn of phrase which seems to dismiss as ineffective both homeopathy and the role of the placebo in healing.

The aim of this short report is to explore the relationship between homeopathy and placebo, how these are connected to self-healing and how we can design a clinical trial to measure these interconnected effects.

Recent insights into the changes associated with placebo may explain why the placebo response trait could be positively selected for during our evolutionary history:

'It is becoming ever more apparent that 'the placebo effect' is polymorphic in both its trigger and its expression, and that the mechanisms for placebo responses within the body are diverse. It is also clear that in all societies healing modalities have developed to maximize

Acknowledgements

The author would like to acknowledge the help of Prof Atholl Johnston, Dr Art Tucker, Dr Carol Rivas, Mrs Virginia Shankland, Dr Len Parkyn, Neil MacLachlan, Dr Neil Elnaggar, Sister Michelle Thomas, Mr and Mrs Roger Wilson and Dr Istvan Zatik

Provenance

Submitted; peer reviewed by Heather Goodare

the placebo response in an attempt to overcome assaults to well being. This raises the question as to whether the placebo response, like other self-healing mechanisms, may be an evolutionary adaptation.¹

Given the extreme plasticity of the human brain in response to experience and the potential differences due to genetic variation, it is clear that the old 'nature vs. nurture' debate has some relevance to our understanding of placebo. If the range of individual placebo responses is wide then this also has implications for the large sample sizes needed for meaningful analysis of clinical trial data.

Methods

The evidence for this review was gathered from a search of the PubMed database (<http://www.ncbi.nlm.nih.gov/pubmed>), using the terms 'homeopathy', 'self-healing' and 'placebo', which yielded 19 published papers.

In order to review the trial design of published trials of homeopathy with a non-treatment group, a PubMed search was conducted using the search terms 'homeopathy' and 'clinical trials' with the filter 'last five years' and excluding surveys with no placebo, animals and plant studies. This generated 41 papers for analysis.

In order to find material about trials that show a specific effect for homeopathy, a PubMed search using the terms 'homeopathy' + 'specific' and filtered to show clinical trials over the last five years in human subject returned only 10 studies.

Additional inspiration and material was sourced at the inaugural meeting of the Pain Medicine Section of the Royal Society of Medicine 'The role of the placebo in clinical care' which was held on Friday 18 November 2011.

Professor Atholl Johnston provided the link to the data on the discovery of the genetic basis for the placebo effect in IBS patients. The information about homeopathy was cited using books from the author's own library and details are included in the bibliography.

Genetic individuality

The individual nature of each patient's response has some basis in genetic variation and this is identified as a fruitful new avenue of research

by Benedetti and Amanzio.² In a recent study from Beth Israel Deaconess Medical Centre (BIDMC) and Harvard Medical School (HMS), scientists claim to have identified genetic differences between people who respond to placebos during trials and those who do not.³

Placebo, semiotics and meaning

Medical or therapeutic treatment happens to unique individuals, each with their own interpretation of the experience. Walach⁴ recognizes that the individual psychological and psychosomatic receptive action on the part of the patient is relevant to therapeutic success.

Meissner *et al.*⁵ confirms that the placebo effect is 'a real neurobiological phenomenon and that the brain's "inner pharmacy" is a critical determinant for the occurrence of psychobiological and behavioral changes relevant to healing processes and wellbeing'.

Meissner⁶ proposes that verbal suggestions during placebo interventions may activate association networks in the brain that store memories of the appropriate autonomic response. Organ functions regulated by the Autonomic Nervous System (ANS) including the cardiovascular, gastrointestinal and pulmonary systems are amenable to both placebo and nocebo interventions.

Benedetti and how placebos change the patient's brain

The 2011 review of neurobiological findings by Benedetti *et al.*⁷ provides a compelling view of placebo as a psychosocial context effect where social stimuli such as words and rituals of the therapeutic act may change the chemistry and circuitry of the patient's brain. Benedetti *et al.* show that drugs are administered into a complex biochemical environment that varies according to the patient's cognitive/affective state and previous exposure to other pharmacological agents. The mechanisms activated by placebo are the same as those activated by drugs, which suggests a cognitive/affective interference with drug actions.

Rather than one common mechanism of action, they suggest that there is a whole 'melting pot' of different placebo effects operate at different times

and under different circumstances. Sometimes anxiety is modulated, at other times reward mechanisms are involved and in other circumstances different types of learning, conditioning or even genetic variants may play a role in placebo responsiveness.

Placebo in relation to evolution

The role of expectation of benefit and the hope of healing have also been examined by Benedetti and Amanzio.² The expectation of future events is known to modulate anxiety and to induce physiological changes through reward mechanisms. The nocebo effect, which is the opposite of the placebo effect, provides some of the best evidence of the role that anxiety plays in placebo responses.

There is a survival value to the ability to prepare the body to anticipate and cope with a future event. The main purpose of perception is to help predict the future,⁸ if expectations about the future change the body's defensive emotional, behavioural and physiological responses then placebo responsiveness could be seen as a trait favoured by natural selection.

From the evolutionary perspective individuals who can protect themselves, heal themselves and recuperate from infections, injury and illness are more likely to survive and reproduce and therefore pass these adaptive traits on to their offspring.

The connection between illness and disease

One of the themes of this approach is the distinction between disease and illness. Disease may be considered to be patho-physiological whereas illness is phenomenological. Illness is the lived experience (emotions) of detriment to health including the symptomatic manifestation of disease. Miller *et al.*⁹ suggest that the placebo effect operates predominantly by producing symptomatic relief of illness rather than modifying the physiology of disease.

The role of the 'healer' in placebo

Because the symptoms of illness have themselves a survival value, it is reasonable to suppose that it

will only be 'safe' to 'turn them off' when sanctioned by a 'healer' or practitioner.

'From a psychodynamic perspective the healer's authority and ability to comfort may be a projection of parental care, operating by a process of transference.'¹⁰

Ernst and Resch¹¹ have noted that procedures intimately involving the patient as well as those that are invasive, like acupuncture or ultrasound are associated with a more powerful true placebo effect than oral drug treatment. In these situations the 'healer' is playing an immediate and active role and the 'patient' is interpreting this as somehow more powerful, direct and significant.

The context of the clinical encounter and the relationship between the healer and the patient are imbued with meaning and enshrined in ritual. Dr Cecil Helman¹² relates how his consulting room is a type of stage-set where small human dramas are played out every day. 'Props, costumes, sets and a precise choreography' achieve the creation of a 'certain atmosphere of belief and expectation'.

Self-healing and homeopathy

'We are inclined to attribute recovery from disease to the ministrations of healers when, in point of fact, it is often due to self-limiting diseases and the automatic natural healing of the organism.'⁹

It is important to distinguish interpersonal healing from two other forms of healing, natural healing and technological healing, because homeopathy is often described as 'natural' and perceived as an alternative to 'technological' healing options:

'Natural healing is the spontaneous or automatic response of the body to disease or injury, exemplified by internal mechanisms of fighting infection and wound healing. Technological healing consists of the full array of medical and surgical treatment that have pharmacological or physiological properties capable of promoting cure, disease control, or symptomatic relief.'⁹

The homeopathic consultation process is a two-way process in which the patient narrative

is received by the therapist and generates questions or reflections. This must involve a psychological transaction between patient and therapist that will be perceived through the frame of their previous experiences. The patient is conscious, active and 'being heard'.

Benedetti has explored the role of the prefrontal cortex in placebo responses and concluded that if prefrontal functioning is impaired, placebo responses are reduced or totally lacking, as occurs in dementia of the Alzheimer's type.⁷

The homeopathic clinical encounter will involve healing on many levels as there will be interpersonal transactions including psychodynamic effects, the ritual associated with consultation and perhaps lifestyle advice and education. The patients may also be receiving concurrent technological healing from their medical practitioners as well as being prescribed a homeopathic preparation to aid 'natural healing'.

The philosophy of homeopathy

The philosophy of homeopathy is built around the concept of vital force, this is understood to be a dynamic life force which 'steers all the functions of life'.¹³ The concept of vital force was introduced by Hahnemann in the early editions of the *Organon*,¹⁴ and is based on the concept of 'Vitalism' which existed at that time.

'The task of the vital force is to maintain harmony and order in the organism. Every component of the organism, every organ and every cell is influenced and guarded by the vital force. The vital force protects us from ill.'¹³

According to this homeopathic approach, the origin of disease lies in the disturbance of this energy matrix not in the organic physical matrix of the body, '*The origins of illness are to be found in the weakened vital force.*'¹³ Healing therefore must also influence this vital force and homeopathic medicines are believed to stimulate and strengthen the vital force to promote self-healing and returning them to equilibrium of mind, body and spirit.

'The goal of homoeopathic treatment is not to directly remove or suppress a symptom rather to strengthen and harmonize the vital force.'¹³

Later homeopaths such as Vithoulkas¹⁵ have elaborated on this concept to propose the primary and secondary action of homeopathic remedies:

'Every agent that acts upon the vitality, every medicine, deranges more or less the vital forces, and causes a certain alteration in the health of the individual for a longer or shorter period. This is termed primary action. Although a product of the medicine and vital powers conjointly, it is principally due to the former power. To its action our vital force endeavors to oppose its own energy. This resistant action is a property, is indeed an automatic action of our life-preserving power, which goes by the name of secondary action or counteraction.'¹⁵

The capacity to self-heal is therefore seen as an innate 'energy' which can be strengthened and stimulated by the application of the homeopathic medicine because the medicine itself has been prepared by a series of dilutions and succussions to reduce its primary effect of medication and awaken its latent dynamic power:

'By means of this manipulation of crude drugs are produced preparations which only in this way reach the full capacity to forcibly influence the suffering parts of the sick organism.'¹⁴ §270

The correct selection of that medicine is of paramount importance because the choice requires the therapies to take a detailed individual case history during which the patient is required to describe their symptoms. It has been suggested¹⁶ that

'The non-specific therapeutic effects of the doctor-patient relationship are likely to be increased by the patient's expectations of the homeopathic method which meshes with the specific therapeutic effects of the medicines.'

Self-healing and homeopathy

It is clear that homeopathy includes the concept of self-healing in its philosophy and practice, and there is a recognition that the ability to self-regulate or return to health is innate in humans.

Homeopaths attribute this to a 'vital force' and believe that this innate process can be aided by the administration of a specially prepared 'remedy' that supports the body in the process.

Homeopathy pays attention to the idea that physical changes relate to a prior 'energetic' change and that good health encompasses spiritual, mental, emotional and physical dimensions (Table 1).

Designing a clinical trial to measure the true placebo effect

An important question remains as to how we separate and measure the specific 'medicine' effects from the non-specific 'brain' effects when we attempt to evaluate homeopathy?

This dilemma was highlighted as early as 1995¹¹ when it was suggested that most authors confuse the *perceived* placebo effect with the *true* placebo effect. The true placebo effect can only be identified by including an untreated control group in clinical trials. By doing so the other non-specific effects that contribute to the perceived placebo effect (such as natural course, regression to the mean, other time effects and unidentified parallel interventions), can be excluded.

Clinical trials

Two types of trial are therefore of interest when considering these issues: those trials of homeopathy that compare a placebo group, active drug group with a no treatment group and trials that seek to reproduce specific effects of homeopathic remedies.

In order to investigate the first group I conducted a PubMed search of published work in the last five years using the keywords Homeopathy and Clinical Trials, excluding surveys with no placebo, and those with animal and plant subjects. Forty trials were identified of which only three (7.5%) included a non-intervention group.

This analysis of the published work shows that only a small percentage of trials of homeopathic medicine use a non-participating control group and that that this kind of group may be used for different reasons. Future studies of homeopathy should seek to include an untreated control group in order to help distinguish the true placebo effect from other nonspecific effects.

Trials that seek to reproduce specific effects of homeopathic remedies

A PubMed search using the terms 'homeopathy' + 'specific' and filtered to show clinical trials over the last five years in human subjects returned only 10 studies (Table 2).

The eczema study¹⁷ showed that both homeopathic and conventional treatment groups improved similarly over a 12-month period but as this was an observational study of a cohort there was no control group and no placebo.

A migraine study¹⁸ showed improvement for patients seeking homeopathic relief but the study was designed to observe real-life conditions and did not aim to determine the specific effect of a homeopathic remedy. The study was also not designed to measure the placebo effect.

The fifth study from the Institute for Social Medicine, Epidemiology and Health Economics; Charité University Medical Center; D-10098 Berlin, Germany, concluded that while their results confirm the toxicological and clinical effects of *Galphimia glauca* compared to placebo, the ICCH criteria for proving symptoms were not suitable to distinguish between specific and unspecific symptoms.

The work of Bell *et al.*^{19,20} explores the role of electroencephalography (EEG) as a sensitive tool for measuring the specific changes due to the administration of homeopathic remedies.

Walach *et al.* take the most direct approach to the question of specific vs. non-specific symptoms of homeopathy. The 2001 study of the effects of homeopathic *Belladonna 30CH* in healthy volunteers²¹ tested the hypothesis that symptoms patterns are due to specific effects of a homeopathic remedy but found no indication that *Belladonna 30CH* produces symptoms different from placebo.

This was followed in 2004 by a pilot study using a small number of participants and the remedy *Cantharis*²² showed that homeopathic proving symptoms appeared to be specific but the trial needed replication. This was achieved in 2008²³ and 2009²⁴ when they used a three-armed, double-blind, placebo-controlled randomized study design in which volunteers took either one of two homeopathic remedies, *Natrum muriaticum* or *Arsenicum album* in 30CH or identical placebo. Their main outcome

Table 1.
PubMed search for homeopathy.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
Multiweek resting EEG cordance change patterns from repeated olfactory activation with two constitutionally salient homeopathic remedies in healthy young adults.	Bell IR, Howerter A, Jackson N, Brooks AJ, Schwartz GE. J Altern Complement Med. 2012 May;18(5):445–53. PMID: 22594648 [PubMed – indexed for MEDLINE]	Ninety-seven young adults ($N = 97$, mean age 19 years, 55% women) with good self-rated global health and screened for homeopathic constitutional types consistent with one of two remedies (either Sulphur or Pulsatilla) underwent three weekly laboratory sessions. At each visit, subjects had 5-min resting, eyes-closed EEG recordings before and after a placebo-controlled olfactory activation task with their constitutionally relevant verum remedy. One remedy potency (6c, 12c, or 30c) used per week, was presented in a randomized order over the three sessions. Prefrontal resting EEG cordance values at Fp1 and Fp2 were computed from artefact-free 2-min EEG samples from the presniffing and postsniffing rest periods. Cordance derives from an algorithm that incorporates absolute and relative EEG values.	No
Frequently occurring polar symptoms assessed by successful cases.	Rutten LA, Frei H. Homeopathy. 2012 Apr;101(2):103–11. PMID: 22487370 [PubMed – indexed for MEDLINE]	In a pilot study 30 questions out of a standard questionnaire in 102 cases responding well to five medicines were analysed and compared with a control group of 100 consecutive new cases. Outcomes of a pivot table, Likelihood Ratio (LR) calculations and Multivariate Analysis (MVA) were compared.	No
Homeopathic medicines substantially reduce the need for clotting factor concentrates in haemophilia patients: results of a blinded placebo controlled cross over trial.	Kundu T, Shaikh A, Kutty A, Nalvade A, Kulkarni S, Kulkarni R, Ghosh K. Homeopathy. 2012 Jan;101(1):38–43. PMID: 22226313 [PubMed – indexed for MEDLINE]	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 one 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.	No

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
Real-life effect of classical homeopathy in the treatment of allergies: a multicenter prospective observational study.	Gründling C, Schimetta W, Frass M. <i>Wien Klin Wochenschr.</i> 2012 Jan;124(1-2):11-17. Epub 2011 Dec 8. PMID: 22138796 [PubMed – indexed for MEDLINE]	A prospective multicenter observational study was conducted by general practitioners specialising in homeopathy in nine Austrian test centres. Personal data and symptoms of allergic patients diagnosed with allergic conjunctivitis, allergic rhinitis, bronchial asthma and neurodermatitis before and after homeopathic treatment were assessed by means of questionnaires (classification of patients' condition by using visual analogue scales/VAS).	No
Management of distress during climacteric years by homeopathic therapy.	Nayak C, Singh V, Singh K, Singh H, Gupta J, Lamba CD, Sharma A, Sharma B, Indira B, Bhuvaneshwari S, Bindra SK, Luxmi KS. <i>J Altern Complement Med.</i> 2011 Nov;17(11):1037-42. PMID: 22087613 [PubMed – indexed for MEDLINE]	An open, multicentre, prospective, observational study was carried out to ascertain the usefulness of homeopathic treatment in distress during climacteric years (DDCY). Patients were enrolled from the general outpatient department of the six Institutes/Units of Central Council for Research in Homeopathy (CCRH) and were required to complete a follow-up period of one year as per the protocol designed by the CCRH. A uniform questionnaire assessing 15 predefined symptoms of menopause was adopted, with assessment of each symptom at every visit. Levels of serum FSH and lipid profile were monitored at entry and at completion. Effect size of the study was also calculated. CARA Software was used for repertorization of the presenting symptoms of menopause along with the characteristic attributes of each patient to arrive at a simillimum. The selected medicine was prescribed in a single dose as per the homeopathic principles. The assessment of the results was made through statistical analysis using the Wilcoxon signed-rank test on Statistical Package for Social Sciences (SPSS) comparing symptom score at entry and completion of one year of treatment and <i>t</i> test for analysing improvement in laboratory findings.	No
Measuring the effectiveness of homeopathic care through objective and shared indicators.	Leone L, Marchitello M, Natili M, Romano MF. <i>Homeopathy.</i> 2011 Oct;100(4):212-19. PMID: 21962195 [PubMed – indexed for MEDLINE]	Indicators of hospitalisation and drug use were obtained from the Health Statistical Documentation System of Tuscany for two homeopathic centres in the Local Health Authority of Pisa, Italy. Compared homeopathic users with the general population in the same area and by comparing patients before and after homeopathic treatment.	Yes

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
An exploratory study on scientific investigations in homeopathy using medical analyzer.	Mishra N, Muraleedharan KC, Paranjpe AS, Munta DK, Singh H, Nayak C. <i>J Altern Complement Med.</i> 2011 Aug;17(8):705–10. PMID: 21787219 [PubMed – indexed for MEDLINE]	Pre- and postinterventional variability spectra of heart rate and blood flow of 77 subjects were recorded with the Medical Analyzer System, administering homeopathic preparations of <i>Aconitum napellus</i> (6 c, 10 M), <i>Arsenicum album</i> (200 c, 1 M), <i>Gelsemium sempervirens</i> (200 c, 1 M), Phosphorus (200 c, 1 M), <i>Pulsatilla nigricans</i> (200 c) and Sulphur (200 c, 1 M) versus placebo control. The amplitude of the peaks viz. low-frequency, medium-frequency, and high-frequency was measured for postintervention analysis. An increase in the amplitude of any valid peak by 100% or a decrease by 50% was considered as significant change.	No
The feasibility of a pragmatic randomised controlled trial to compare usual care with usual care plus individualised homeopathy, in children requiring secondary care for asthma.	Thompson EA, Shaw A, Nichol J, Hollinghurst S, Henderson AJ, Thompson T, Sharp D. <i>Homeopathy.</i> 2011 Jul;100(3):122–30. PMID: 21784328 [PubMed – indexed for MEDLINE]	In a pragmatic parallel group randomised controlled trial (RCT) design, children on step 2 or above of the British Thoracic Society Asthma Guidelines (BTG) were randomly allocated to UC or UC plus a five visit package of homeopathic care (HC). Outcome measures included the Juniper Asthma Control Questionnaire, Quality of Life Questionnaire and a resource use questionnaire. Qualitative interviews were used to gain families' and health professionals' views and experiences.	No
Homeopathic Plumbum metallicum for lead poisoning: a randomized clinical trial.	Padilha RQ, Riera R, Atallah AN. <i>Homeopathy.</i> 2011 Jul;100(3):116–21. PMID: 21784327 [PubMed – indexed for MEDLINE]	Double-blind randomized trial.	No
Homeopathic ear drops as an adjunct to standard therapy in children with acute otitis media.	Taylor JA, Jacobs J. <i>Homeopathy.</i> 2011 Jul;100(3):109–15. PMID: 21784326 [PubMed – indexed for MEDLINE]	Children with AOM were enrolled in the study at the time of diagnosis and randomised to receive either standard therapy alone or standard therapy plus a homeopathic ear drop solution that was to be used on as needed basis for up to five days. Parents of children in both treatment groups rated the severity of 5 AOM symptoms twice daily for five days in a symptom diary. A symptom score was computed for each assessment with lower scores denoting less severe symptoms. Parents of children randomised to receive ear drops also recorded information regarding symptoms being treated and response to treatment.	No

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
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.	Khuda-Bukhsh AR, Banerjee A, Biswas SJ, Karmakar SR, Banerjee P, Pathak S, Guha B, Haque S, Das D, De A, Das D, Boujedaini N. Xi Z, He YJ and Bao X. 2011 Jun;9(6):596–604. PMID: 21669162 [PubMed – indexed for MEDLINE]	This study was carried out on volunteers living in an arsenic-affected village where no arsenic-free drinking water is available. Twenty-eight volunteers from the village of Dasdiya, in Haringhata block under Nadia District, West Bengal, India, an arsenic-contaminated village where wells contain 55 to 95 µg/L arsenic, were selected to undertake a double-blind and placebo-controlled trial. The subjects provided samples of blood and urine before and after two months of taking either 'verum' or 'placebo'. Another 18 subjects living in an arsenic-free village served as the negative controls.	Yes
Pulpa dentis D30 for acute reversible pulpitis: a prospective cohort study in routine dental practice.	Hamre HJ, Mittag I, Glockmann A, Kiene H, Tröger W. Altern Ther Health Med. 2011 Jan–Feb;17(1):16–21. PMID: 21614940 [PubMed – indexed for MEDLINE]	Prospective, observational, open-label, single-arm cohort study.	No
Homeopathy for depression – DEPHOM: study protocol for a randomized, partially double-blind, placebo controlled, four armed study.	Adler UC, Krüger S, Teut M, Lüdtke R, Bartsch I, Schützler L, Melcher F, Willich SN, Linde K, Witt CM. Trials. 2011 Feb 14;12(1):43. PMID: 21320338 [PubMed – indexed for MEDLINE]	A randomised, partially double-blind, placebo-controlled, four-armed trial using a 2 × 2 factorial design with a six-week study duration per patient will be performed. 228 patients diagnosed with major depression (moderate episode) by a psychiatrist will be included. The primary endpoint is the total score on the 17-item Hamilton Depression Rating Scale after six weeks. Secondary end points are: Hamilton Depression Rating Scale total score after two and four weeks; response and remission rates, Beck Depression inventory total score, quality of life and safety at two, four and six weeks. Statistical analyses will be by intention-to-treat. The main endpoint will be analysed by a two-factorial analysis of covariance. Within this model generalised estimation equations will be used to estimate differences between verum and placebo, and between both types of case history.	No

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
Homeopathy has clinical benefits in rheumatoid arthritis patients that are attributable to the consultation process but not the homeopathic remedy: a randomized controlled clinical trial.	Brien S, Lachance L, Prescott P, McDermott C, Lewith G. <i>Rheumatology</i> (Oxford). 2011 Jun;50(6):1070–82. Epub 2010 Nov 13. PMID: 21076131 [PubMed] – indexed for MEDLINE]	Exploratory double-blind, randomised placebo-controlled trial conducted from January 2008 to July 2008, in patients with active stable RA receiving conventional therapy. Eighty-three participants from three secondary care UK outpatient clinics were randomized to 24 weeks of treatment with either homeopathic consultation (further randomized to individualized homeopathy, complex homeopathy or placebo) or non-homeopathic consultation (further randomized to complex homeopathy or placebo). Co-primary outcomes: ACR 20% improvement (ACR20) criteria and patient monthly global assessment (GA). Secondary outcomes: 28-joint DAS (DAS-28), tender and swollen joint count, disease severity, pain, weekly patient and physician GA and pain, and inflammatory markers.	No
Effects of homeopathic medicines on polysomnographic sleep of young adults with histories of coffee-related insomnia.	Bell IR, Howerter A, Jackson N, Aickin M, Baldwin CM, Bootzin RR. <i>Sleep Med</i> . 2011 May;12(5):505–11. Epub 2010 Jul 29. PMID: 20673648 [PubMed] – indexed for MEDLINE]	Young adults of both sexes (ages 18–31) with above-average scores on standardized personality scales for either cynical hostility or anxiety sensitivity (but not both) and a history of coffee-induced insomnia participated in the month-long study. At-home polysomnographic recordings were obtained on successive pairs of nights once per week for a total of eight recordings (nights 1, 2, 8, 9, 15, 16, 22, 23). Subjects (N=54) received placebo pellets on night 8 (single-blind) and verum pellets on night 22 (double-blind) in 30 c doses of one of two homeopathic remedies, Nux Vomica or Coffea Cruda. Subjects completed daily morning sleep diaries and weekly Pittsburgh sleep quality index scales, as well as profile of mood states scales at bedtime on polysomnography nights.	No
Protocol for a phase 1 homeopathic drug proving trial.	Teut M, Hirschberg U, Luedtke R, Schnegg C, Dahler J, Albrecht H, Witt CM. <i>Trials</i> . 2010 Jul 22;11:80. PMID: 20649979 [PubMed] – indexed for MEDLINE]	Multi-centre, randomised, double-blind, placebo-controlled phase 1 trial with 30 healthy volunteers. The study consists of a seven day run-in period, a five-day intervention period and a 16-day post-intervention observation period. Subjects, investigators and the statisticians are blinded from the allocation to the study arm and from the identity of the homeopathic drug. The intervention is a highly diluted homeopathic drug (potency C12 = 1024). Dose: five globules taken five times per day over a maximum period of five days.	No

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
Homeopathic treatment of patients with migraine: a prospective observational study with a 2-year follow-up period.	Witt CM, Lüttke R, Willich SN. <i>J Altern Complement Med.</i> 2010 Apr;16(4):347–55. PMID: 20423206 [PubMed – indexed for MEDLINE]	The placebo consists of an optically identical carrier substance (sucrose globules). Subjects document the symptoms they experience in a semi-structured online diary. The primary outcome parameter is the number of specific symptoms that characterise the intervention compared to the placebo after a period of three weeks. Secondary outcome parameters are qualitative differences in profiles of characteristic and proving symptoms and the total number of all proving symptoms. The number of symptoms will be quantitatively analysed on an intention-to-treat basis using ANCOVA with the subject's expectation and baseline values as covariates. Content analysis according to Mayring is adapted to suit the homeopathic qualitative analysis procedure.	No
Traumeel S for pain relief following hallux valgus surgery: a randomized controlled trial.	Singer SR, Amit-Kohn M, Weiss S, Rosenblum J, Maoz G, Samuels N, Lukaszewicz E, Freedman L, Paltiel O, Itzhaki M, Niska M, Oberbaum M. <i>BMC Clin Pharmacol.</i> 2010 Apr 12;10:9. PMID: 20380750 [PubMed – indexed for MEDLINE]	This was a prospective multicenter observational study. Consecutive patients beginning homeopathic treatment in primary care practices were evaluated over two years using standardized questionnaires. The data recorded included diagnoses (International Classification of Diseases, Ninth Revision) and current complaints, including their severity (numeric rating scale = 0–10), health-related quality of life (QoL, 36-item Short-Form Health Survey), medical history, consultations, homeopathic and conventional treatments, as well as other health service use. We performed a randomized, double-blind, placebo-controlled trial to evaluate the efficacy of the homeopathic preparation Traumeel S in minimising post-operative pain and analgesic consumption following surgical correction of hallux valgus. Eighty consecutive patients were randomized to receive either Traumeel tablets or an indistinguishable placebo, and took primary and rescue oral analgesics as needed. Maximum numerical pain scores at rest and consumption of oral analgesics were recorded on day of surgery and for 13 days following surgery.	No

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
No effect of a homeopathic combination of <i>Arnica montana</i> and <i>Bryonia alba</i> on bleeding, inflammation, and ischaemia after aortic valve surgery.	Cornu C, Joseph P, Gaillard S, Bauer C, Vedrinne C, Bissery A, Melot G, Bossard N, Belon P, Lehot JJ. <i>Br J Clin Pharmacol.</i> 2010 Feb;69(2):136–42. PMID: 20233176 [PubMed – indexed for MEDLINE]	One day before surgery, 92 adult patients were randomly assigned to a double-blind parallel trial with either homeopathic granules or a matching placebo until 4 days after surgery. The primary outcome was the volume of blood/liquid in the drains at their removal. The secondary outcomes included postoperative blood/liquid losses at 12 and 24 h as well as C-reactive protein (CRP), pain, temperature and plasma troponin I _c .	No
Homeopathic treatment of elderly patients – a prospective observational study with follow-up over a two year period.	Teut M, Lütke R, Schnabel K, Willich SN, Witt CM. <i>BMC Geriatr.</i> 2010 Feb 22;10:10. PMID: 20175887 [PubMed – indexed for MEDLINE]	In this subgroup analysis of a prospective, multicentre cohort study totally including 3981 patients treated by homeopathic physicians in primary care practices in Germany and Switzerland, data was analysed from all patients >70 years consulting the physician for the first time. The main outcome measures were: assessment by patient of the severity of complaints (numeric rating scales) and quality of life (SF-36) and by the physician of the severity of diagnoses (numeric rating scales) at baseline, and after 3, 12, and 24 months.	No
Chronic primary insomnia: efficacy of homeopathic <i>simillimum</i> . Naudé DF, Stephanie Couchman IM, Maharaj A.	Homeopathy. 2010 Jan;99(1):63–8. Erratum in: Homeopathy. 2010 Apr;99(2):151. PMID: 20129178 [PubMed – indexed for MEDLINE]	30 participants were selected in accordance with DSM-IV TR (2000) (1) criterion 307.42 Primary Insomnia and then randomly divided between treatment and placebo groups. The measurement tools used were a Sleep Diary (SD) and the Sleep Impairment Index (SII). (2) After an initial consultation, two follow-up consultations at two-week intervals took place. Homeopathic medication was prescribed at the first and second consultations. The SII was completed at each consultation and participants were instructed at the first consultation to start the SD.	No
[Effectiveness of a classical homeopathic treatment in atopic eczema. A randomised placebo-controlled double-blind clinical trial].	Siebenwirth J, Lütke R, Remy W, Rakoski J, Borelli S, Ring J. <i>Forsch Komplementmed.</i> 2009 Oct;16(5):315–23. Epub 2009 Sep 3. German. PMID: 19887810 [PubMed – indexed for MEDLINE]	Single-centre, randomised, double-blind clinical trial comparing homeopathic remedies with placebo in young adults (age 18–35) with atopic dermatitis. Homeopathic remedies were individually administered according to the rules of classical homeopathy. After an untreated baseline period of four weeks, all patients were treated and monitored for 32 weeks. Throughout the study, co-medication was allowed	No

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
Homeopathic versus conventional therapy for atopic eczema in children: medical and economic results.	Witt CM, Brinkhaus B, Pach D, Reinhold T, Wruck K, Roll S, Jäckel T, Staab D, Wegscheider K, Willich SN. <i>Dermatology</i> . 2009;219(4):329–40. Epub 2009 Oct 13. PMID: 19828937 [PubMed – indexed for MEDLINE]	only with indifferent emollients. The main outcome parameter was disease severity as assessed by Costa and Saurat's multi-parameter atopic dermatitis score (MP-score). In a prospective multicentre comparative observational non-randomised study, 135 children (homeopathy $n = 48$ vs. conventional $n = 87$) with mild to moderate atopic eczema were included. The primary outcome was the SCORAD (Scoring Atopic Dermatitis) at 6 months. Further outcomes at six and 12 months also included quality of life of parents and children, use of conventional medicine, treatment safety and disease-related costs.	No
Effectiveness of the homeopathic preparation Neurexan compared with that of commonly used valerian-based preparations for the treatment of nervousness/restlessness – an observational study.	Hubner R, van Haselen R, Klein P. <i>ScientificWorldJournal</i> . 2009 Aug 11;9:733–45. PMID: 19705035 [PubMed – indexed for MEDLINE]	A prospective, nonrandomized, noninterventive, observational study, using conventional or CAM practices, was conducted in 49 German practices. Each practice could include up to 15 subjects treated with either the homeopathic preparation Neurexan or with combination formulations based on valerian extracts. There was no placebo group.	No
Homeopathic treatment of minor aphthous ulcer: a randomized, placebo-controlled clinical trial.	Mousavi F, Mojaver YN, Asadzadeh M, Mirzazadeh M. <i>Homeopathy</i> . 2009 Jul;98(3):137–41. PMID: 19647206 [PubMed – indexed for MEDLINE]	A randomized, single blind, placebo-controlled clinical trial of individualised homeopathy. One hundred patients with minor aphthous ulcer were treated with individualised homeopathic medicines or placebo and followed up for six days. Patients received two doses of individualised homeopathic medicines in the 6 C potency as oral liquid at baseline and 12 h later. Pain intensity and ulcer size were recorded at baseline during and at the end of the trial (mornings of days 4 and 6).	No
Monthly itraconazole versus classic homeopathy for the treatment of recurrent vulvovaginal candidiasis: a randomised trial.	Witt A, Kaufmann U, Bitschnau M, Tempfer C, Ozbal A, Haytouglu E, Gregor H, Kiss H. <i>BJOG</i> . 2009 Oct;116(11):1499–505. Epub 2009 Jul 7. PMID: 19583713 [PubMed – indexed for MEDLINE]	Women were randomised into three groups: itraconazole with lactobacilli (group 1), itraconazole without lactobacilli (group 2) and CH (group 3). Itraconazole treatment of acute infection was followed by a 6-month maintenance regimen with monthly single-day itraconazole (200 mg bid). Women in group 1 were given additional vaginal lactobacilli for 6 days per month throughout the maintenance regimen. Thereafter, patients were followed without treatment for six months. CH treatment was performed for 12 months	No

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
Homeopathic pathogenetic trials produce specific symptoms different from placebo.	Möllinger H, Schneider R, Walach H. <i>Forsch Komplementmed.</i> 2009 Apr;16(2):105–10. Epub 2009 Apr 9. PMID: 19420956 [PubMed – indexed for MEDLINE]	Three armed, double-blind, placebo controlled randomised experimental pathogenetic study in 25 healthy volunteers who took either one of two homeopathic remedies, Natrum muriaticum and Arsenicum album in 30CH or identical placebo. Main outcome parameter was the number of remedy-specific symptoms per group.	No
Healthcare provided by a homeopath as an adjunct to usual care for Fibromyalgia (FMS): results of a pilot Randomised Controlled Trial.	Relton C, Smith C, Raw J, Walters C, Adebajo AO, Thomas KJ, Young TA. <i>Homeopathy.</i> 2009 Apr;98(2):77–82. PMID: 19358959 [PubMed – indexed for MEDLINE]	In a pragmatic parallel group RCT design, adults with a diagnosis of FMS (ACR criteria) were randomly allocated to usual care or usual care plus adjunctive care by a homeopath. Adjunctive care consisted of five in depth interviews and individualised homeopathic medicines. The primary outcome measure was the difference in Fibromyalgia Impact Questionnaire (FIQ) total score at 22 weeks.	No
Homeopathic treatment of patients with dysmenorrhea: a prospective observational study with 2 years follow-up.	Witt CM, Lütke R, Willich SN. <i>Arch Gynecol Obstet.</i> 2009 Oct;280(4):603–11. Epub 2009 Feb 20. PMID: 19229544 [PubMed – indexed for MEDLINE]	Prospective multicenter observational study in primary care, using standardized questionnaires to record for two years diseases, quality of life, medical history, consultations, all treatments, other health services use.	No
Ignatia in the treatment of oral lichen planus.	Mousavi F, Sherafati S, Mojaver YN. <i>Homeopathy.</i> 2009 Jan;98(1):40–4. PMID: 19135958 [PubMed – indexed for MEDLINE]	In this single blind randomized control clinical trial, 30 consecutive patients with oral lesions consistent clinically and histologically with erosive and/or atrophic OLP were recruited. The patients were randomly divided into two groups to receive Ignatia or placebo. They were treated for four months.	No
Evaluation of the quality of life after individualized homeopathic treatment for seasonal allergic rhinitis. A prospective, open, non-comparative study.	Goossens M, Laekeman G, Aertgeerts B, Buntinx F. <i>ARCH study group. Homeopathy.</i> 2009 Jan;98(1):11–16. PMID: 19135954 [PubMed – indexed for MEDLINE]	A prospective, open, non-comparative study was conducted in Belgium. Patients aged between 14 and 68 years with SAR were treated by one of seven homeopathic physicians. Patients completed the RQLQ at baseline and again after three and four weeks of homeopathic treatment.	No

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
How healthy are chronically ill patients after eight years of homeopathic treatment? – Results from a long term observational study.	Witt CM, Lüdtke R, Mengler N, Willich SN. BMC Public Health. 2008 Dec 17;8:413. PMID: 19091085 [PubMed – indexed for MEDLINE]	In a prospective, multicentre cohort study with 103 homeopathic primary care practices in Germany and Switzerland, data from all patients (age > 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 two and eight years.	No
A homeopathic proving of Galphimia glauca.	Teut M, Dahler J, Schnegg C; Wisede Study Group for Homeopathic Proving. Forsch Komplementmed. 2008 Aug;15(4):211–17. Epub 2008 Aug 15. PMID: 18787330 [PubMed – indexed for MEDLINE]	Randomised, double-blind, placebo-controlled trial with a one-week baseline, four-week proving, and two-week post-observational period. Subjects: 15 healthy physicians and medical students volunteered as provers; 11 were randomised to verum and four to placebo. Proving substance: galphimia glauca C12 compared to placebo; maximum intake of five days. Outcome measures: proving symptoms according to ICCH definition and the number of proving symptoms. The proving symptoms were analysed qualitatively using the Boeninghausen method.	No
Homeopathic pathogenetic trials produce more specific than non-specific symptoms: results from two double-blind placebo controlled trials.	Walach H, Möllinger H, Sherr J, Schneider R. J Psychopharmacol. 2008 Jul;22(5):543–52. PMID: 18701641 [PubMed – indexed for MEDLINE]	We conducted two parallel, blinded homeopathic pathogenetic trials conducted at two different sites to determine whether symptoms reported by healthy volunteers were significantly different for homeopathic remedies than for placebos. Study 1 used a two-armed design, testing ozone against placebo. Study 2 used a three-armed design, testing ozone and iridium against placebo.	No
The role of a homeopathic preparation compared with conventional therapy in the treatment of injuries: an observational cohort study.	Schneider C, Schneider B, Hanisch J, van Haselen R. Complement Ther Med. 2008 Feb;16(1):22–7. Epub 2007 Jul 12. PMID: 18346625 [PubMed – indexed for MEDLINE]	Multi-centre, prospective, comparative observational cohort study of patients with various musculoskeletal injuries. German physicians who were using homeopathy in addition to conventional medicine included patients. Patients treated with Traumeel were compared with patients managed conventionally. The primary outcome measure was the rate of resolution of the principal symptoms (i.e. pain and inflammatory symptoms) at the end of therapy.	No because there could be a placebo effect in both groups so there is no control for placebo

(continued)

Table 1.
Continued.

Title	Authors and reference	Trial design	Non-treatment group used as a comparison
Effect of homeopathy on analgesic intake following knee ligament reconstruction: a phase III monocentre randomized placebo controlled study.	Paris A, Gonnet N, Chaussard C, Belon P, Rocourt F, Saragaglia D, Cracowski JL. <i>Br J Clin Pharmacol.</i> 2008 Feb;65(2):180–7. PMID: 18251757 [PubMed – indexed for MEDLINE]	This was an add-on randomized controlled study with three parallel groups: a double-blind homeopathic or placebo arm and an open-label noninterventional control arm. Eligible patients were 18–60 years old candidates for surgery of the anterior cruciate ligament. Treatment was administered the evening before surgery and continued for three days. The primary end-point was cumulated morphine intake delivered by PCA during the first 24 h inferior or superior/equal to 10 mg day ⁻¹ (–1).	Yes
The effect of adding homeopathic treatment to rehabilitation on muscle tone of children with spastic cerebral palsy.	Sajedi F, Alizad V, Alaeddini F, Fatemi R, Mazaherinezhad A. <i>Complement Ther Clin Pract.</i> 2008 Feb;14(1):33–7. Epub 2007 Dec 27. PMID: 18243940 [PubMed – indexed for MEDLINE]	This study was a double-blind clinical trial. Twenty-four subjects were recruited from a developmental disorders clinic in Tehran in 2004. Subjects were divided into case and control groups. The routine rehabilitation techniques were carried out for four months on both the groups. The control group received placebo and the case group received homeopathy drugs. Both groups were evaluated and compared for muscle tone before and four months after treatment using the Modified Ashworth Scale.	No
Treating hot flushes in menopausal women with homeopathic treatment – results of an observational study.	Bordet MF, Colas A, Marijnen P, Masson J, Trichard M. <i>Homeopathy.</i> 2008 Jan;97(1):10–15. PMID: 18194760 [PubMed – indexed for MEDLINE]	Open, multi-national prospective, pragmatic and non-comparative observational study of homeopathic treatments prescribed and their effectiveness, observing their impact on quality of life.	No
Homotoxicological remedies versus desmopressin versus placebo in the treatment of enuresis: a randomised, double-blind, controlled trial.	Ferrara P, Marrone G, Emanuele V, Nicoletti A, Mastrangelo A, Tiberi E, Ruggiero A, Fasano A, Paolini Paoletti F. <i>Pediatr Nephrol.</i> 2008 Feb;23(2):269–74. Epub 2007 Feb 20. PMID: 17310359 [PubMed – indexed for MEDLINE]	The aim of this trial was to compare the safety and efficacy of homotoxicological remedies versus placebo and versus desmopressin (dDAVP) in the treatment of monosymptomatic nocturnal enuresis (MNE). We conducted a randomised, double-blind, double-dummy, controlled trial in which 151 children with MNE were randomly assigned to receive oral homotoxicological remedies ($n = 50$), dDAVP ($n = 50$) or placebo ($n = 51$)	No

Filters activated: 'published in the last 5 years', 'Clinical Trial'. Animal and plant studies excluded as well as studies based upon a questionnaire where no placebo controlled trial occurred.

Table 2.
PubMed search for 'homeopathy' + 'specific'.

No.	Title of study	Author	Source
1	Multisite resting EEG cordance change patterns from repeated olfactory activation with two constitutionally salient homeopathic remedies in healthy young adults	Bell IR, Howter A, Jackson N, Brooks AJ, Schwartz GE. Source Department of Family & Community Medicine, The University of Arizona, College of Medicine, Tucson, AZ 85719, USA. ibell@email.arizona.edu	J Altern Complement Med. 2012 May;18(5):445-53. doi: 10.1089/acm.2011.0931
2	Short-term effects of repeated olfactory administration of homeopathic sulphur or pulsatilla on electroencephalographic alpha power in healthy young adults	Bell IR, Brooks AJ, Howter A, Jackson N, Schwartz GE. Source Department of Family & Community Medicine, The University of Arizona College of Medicine, 1450 N Cherry Avenue, Tucson, AZ 85719, USA. ibell@email.arizona.edu	Homeopathy. 2011 Oct;100(4):203-11. doi: 10.1016/j.homp.2011.06.005.
3	Homeopathy for depression – DEPHOM: study protocol for a randomized, partially double-blind, placebo controlled, four armed study.	Adler UC, Krüger S, Teut M, Lütke R, Bartsch I, Schützler L, Melcher F, Willich SN, Linde K, Witt CM. Source Institute for Social Medicine, Epidemiology and Health Economics; Charité University Medical Center, D-10098 Berlin, Germany. ubiratan.adler@charite.de	Trials. 2011 Feb 14;12(1):43. doi: 10.1186/1745-6215-12-43.
4	Protocol for a phase 1 homeopathic drug proving trial.	Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, Berlin, Germany. michael.teut@charite.de	Trials. 2010 Jul 22;11:80. doi: 10.1186/1745-6215-11-80.
5	Homeopathic treatment of patients with migraine: a prospective observational study with a 2-year follow-up period.	Witt CM, Lütke R, Willich SN. Source Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, Berlin, Germany. claudia.witt@charite.de	J Altern Complement Med. 2010 Apr;16(4):347-55. doi: 10.1089/acm.2009.0376.
6	Homeopathic pathogenetic trials produce specific symptoms different from placebo.	Möllinger H, Schneider R, Walach H. Source Department of Human Sciences, University of Osnabrück, Germany.	Forsch Komplementmed. 2009 Apr;16(2):105-10. doi: 10.1159/000209386. Epub 2009 Apr 9.
7	Disclosure to physicians of CAM use by breast cancer patients: findings from the Women's Healthy Eating and Living Study.	Department of Family and Preventive Medicine, Moores UCSD Cancer Center, Cancer Prevention and Control, University of California San Diego, La Jolla, CA 92093-0901, USA. gsaxe@ucsd.edu	Integr Cancer Ther. 2008 Sep;7(3):122-9.

(continued)

Table 2.
Continued.

No.	Title of study	Author	Source
8	A homeopathic proving of Galphimia glauca.	Teut M, Dahler J, Schnegg C; Wilsede Study Group for Homeopathic Proving. Source Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, Berlin, Germany. michael.teut@charite.de	Forsch Komplementmed. 2008 Aug;15(4):211–17. doi: 10.1159/000148825. Epub 2008 Aug 15.
9	Homeopathic pathogenetic trials produce more specific than non-specific symptoms: results from two double-blind placebo controlled trials.	Walach H, Möllinger H, Sherr J, Schneider R. Source School of Social Sciences and European Office of the Samueli Institute for Information Biology, University of Northampton, Northampton, UK. harald.walach@northampton.ac.uk	J Psychopharmacol. 2008 Jul;22(5):543–52. doi: 10.1177/0269881108091259.
10	Homeopathic versus conventional treatment of children with eczema: a comparative cohort study.	Keil T, Witt CM, Roll S, Vance W, Weber K, Wegscheider K, Willich SN. Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center Berlin, D-10098 Berlin, Germany. thomas.keil@charite.de	Complement Ther Med. 2008 Feb;16(1):15–21. doi: 10.1016/j.ctim.2006.10.001. Epub 2006 Dec 27.

parameter was the number of remedy-specific symptoms per group. They concluded that homeopathic remedies do produce different symptoms from placebo.

The specific effects of the homeopathic consultation itself have been examined by Brien *et al.*²⁵ who conducted a double-blind, randomized placebo-controlled trial in patients with active stable rheumatoid arthritis (RA). They concluded that the impact of the homeopathic consultation is of clinical relevance to patients and clinicians and that a further study would be justified.

References

1. Thompson JJ, Ritenbaugh C, Nichter M. Reconsidering the placebo response from a broad anthropological perspective. *Cult Med Psychiatry* 2009;33:112–52
2. Benedetti F, Amanzio M. The placebo response: how words and rituals change the patient's brain. *Patient Educ Couns* 2011;84:413–19
3. Pharma.com, O. Genetic 'placebo response' marker has trial design implications say researchers, 2012, <http://www.outsourcing-pharma.com/Clinical-Development/Genetic-placebo-response-marker-has-trial-design-implications-say-researchers>.
4. Walach H. Placebo controls: historical, methodological and general aspects. *Philos Trans R Soc Lond B Biol Sci* 2011;366:1870–8
5. Meissner K, Kohls N, Colloca L. Introduction to placebo effects in medicine: mechanisms and clinical implications. *Philos Trans R Soc Lond B Biol Sci* 2011;366:1783–9
6. Meissner K. The placebo effect and the autonomic nervous system: evidence from an intimate relationship. *Philos Trans R Soc Lond B Biol Sci* 2011;366:1808–17
7. Benedetti F, Carlino E, Pollo A. How placebos change the patient's brain. *Neuropsychopharmacology* 2011;36:339–54
8. John-Smith PS. *The evolutionary basis of placebo, a new approach. The role of the placebo in clinical care*. London, UK: The Royal Society of Medicine, 2011
9. Miller FG, Colloca L, Kaptchuk TJ. The placebo effect: illness and interpersonal healing. *Perspect Biol Med* 2009;52:518–39
10. Brody HM. *Placebos and the philosophy of medicine*. Chicago, IL: University of Chicago Press, 1980
11. Ernst E, Resch KL. Concept of true and perceived placebo effects. *BMJ* 1995;311:551–3
12. Helman C. *Suburban Shaman*. London, UK: Hammersmith Press Ltd., 2004
13. Grollmann H, Maurer U. *Understanding classical homeopathy*. Baar, Switzerland: Groma Verlag, 2002
14. Hahnemann S. *Organon of medicine*. New Delhi: B. Jain Publishers Ltd., 1824
15. Vithoulkas G. Homeopathy: past, present and future. *Br J Clin Pharmacol* 1998;45:613
16. Teixeira MZ, Guedes CH, Barreto PV, Martins MA. The placebo effect and homeopathy. *Homeopathy* 2010;99:119–29

17. Keil T, Witt CM, Roll S, *et al.* Homeopathic versus conventional treatment of children with eczema: a comparative cohort study. *Complement Ther Med* 2008;16:15–21
18. Witt CM, Ludtke R, Willich SN. Homeopathic treatment of patients with migraine: a prospective observational study with a 2-year follow-up period. *J Altern Complement Med* 2010;16:347–55
19. Bell IR, Howerter A, Jackson N, Brooks AJ, Schwartz GE. Multiweek resting EEG cordance change patterns from repeated olfactory activation with two constitutionally salient homeopathic remedies in healthy young adults. *J Altern Complement Med* 2012;18:445–53
20. Bell IR, Brooks AJ, Howerter A, Jackson N, Schwartz GE. Short-term effects of repeated olfactory administration of homeopathic sulphur or pulsatilla on electroencephalographic alpha power in healthy young adults. *Homeopathy* 2011;100:203–11
21. Walach H, Koster H, Hennig T, Haag G. The effects of homeopathic belladonna 30CH in healthy volunteers – a randomized, double-blind experiment. *J Psychosom Res* 2001;50:155–60
22. Walach H, Sherr J, Schneider R, Shabi R, Bond A, Rieberer G. Homeopathic proving symptoms: result of a local, non-local, or placebo process? A blinded, placebo-controlled pilot study. *Homeopathy* 2004;93:179–85
23. Walach H, Mollinger H, Sherr J, Schneider R. Homeopathic pathogenetic trials produce more specific than non-specific symptoms: results from two double-blind placebo controlled trials. *J Psychopharmacol* 2008;22:543–52
24. Mollinger H, Schneider R, Walach H. Homeopathic pathogenetic trials produce specific symptoms different from placebo. *Forsch Komplementmed* 2009;16:105–10
25. Brien S, Lachance L, Prescott P, Mcdermott C, Lewith G. Homeopathy has clinical benefits in rheumatoid arthritis patients that are attributable to the consultation process but not the homeopathic remedy: a randomized controlled clinical trial. *Rheumatology (Oxford)* 2011;50:1070–82

© 2013 The Author(s)

This is an open-access article distributed under the terms of the Creative Commons Attribution Non-commercial License (<http://creativecommons.org/licenses/by-nc/2.0/>), which permits non-commercial use, distribution and reproduction in any medium, provided the original work is properly cited.