



REPORT

Research working group (RWG)

of the

LIGA MEDICORUM HOMOEOPATHICA INTERNATIONALIS (LMHI)

about

Clinical Efficacy of Homeopathy

This report is a response to the Belgian KCE report
evaluating clinical efficacy of homeopathy

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Introduction:

The **Liga Medicorum Homeopathica Internationalis** (LMHI) is an international homeopathic medical society established in Rotterdam on September 10, 1925, under the terms of Swiss Civil Law, stipulating Geneva as its registered office.

The official bodies of the LMHI, frequently termed simply the Liga, include the Executive Committee, the General Secretariat and the International Council which meet annually.

Executive Committee

The Executive Committee is composed of the President, Vice President, Immediate Past President, General Secretary, Veterinary Treasurer, and the other secretaries (for Archives, Dentistry, Education, Pharmacy, Public Relations, Research); it manages the business of the association.

International Council

The International Council is the highest authority of the association: it is composed of the National Vice-Presidents, the links between the LMHI and the national community of homeopathic doctors, pharmacists, veterinarians, etc.

Research Working Group

The Research Working Group is a group of international researchers, coordinated by the elected Research secretary, aimed at giving scientific expert advice to the LMHI.



Report motivation:

This LMHI RWG report has been requested by the Belgian LMHI Vice-president, Dr Léon Scheepers. He asked for scientific advice about an official Belgian report published by the KCE (Centre fédéral d'expertise des soins de santé – Federaal Kenniscentrum voor de gezondheidszorg). That report was published on 24th of May 2011 as KCE report 154B, Homeopathy: State of affairs in Belgium. www.kce.fgov.be

The UNIO HOMEOPATHICA BELGICA expresses some doubts about the scientific relevancy of some parts of the KCE report, especially the part evaluating clinical efficacy concluding that “no convincing proof of efficacy exists for any condition for which a systematic review was available”.

The RWG agreed to scrutinize and comment on this report using the normal scientific perspective for evaluation of efficacy in medicine.

KCE methodology for evaluating clinical efficacy of Homeopathy

The KCE developed a specific methodology to review the scientific literature restricted to documents evaluating the efficacy of homeopathy. Because homeopathy involves an important number of conditions and proposed numerous remedies, they limited their review to systematic reviews. Therefore, only conditions for which they could find at least one systematic review were included. Moreover, they concentrated on reviews of randomized controlled trials (p.13 – 2.1).

HTA (Health Technology Assessment) reports and systematic reviews were selected according to the following criteria: Patients suffering from any condition; Homeopathy; Any comparison (alternative intervention, placebo); Patient relevant outcomes such as mortality, morbidity, quality of life; HTA reports or systematic reviews.

Narrative reviews, editorials, letters, primary studies, economic evaluations. Only publications in English, French, German, Dutch, Spanish or Portuguese were eligible for inclusion in the present report. Other languages were thus excluded. Search date of the review ending before the year 2000.

Quality assessment was made looking at 8 items: adequate research question, adequate literature search, adequate selection, adequate quality appraisal, adequate data-extraction, characteristics of primary studies, adequate handling of clinical and statistical heterogeneity, correct statistical pooling.

In addition, when several systematic reviews were available on a specific sub-topic, the findings of the systematic review with the highest quality rating, most recent literature search or most comprehensive scope (in that order of importance) were reported and were compared between each other.



RWG comments on KCE methodology:

Evidence based medicine (EBM) normally considers different levels of evidence (ref. : [Sackett et al, 1996](#); [Rosenberg et Sackett, 1996](#), [Rosenberg et Donald, 1995](#)), the lowest level being expert advice, the highest being the systematic review of randomized controlled trials (RCTs). In between these extremes, cohort studies are relevant. For some medical approaches it is impossible to reach the highest level of evidence (surgery, psychiatry etc.) and a lower level can be accepted following specific statistical approaches as those based on Bayes theorem. Homeopathy is mainly an individualized approach to the symptoms of each specific patient; as such the conventional diagnosis is not a primary focus. Changes in the symptoms and global health amelioration are more specific.

The BMJ (<http://clinicalevidence.bmj.com/ceweb/about/knowledge.jsp>) stated that the categorisation of *Unknown effectiveness* often reflects difficulties in conducting RCTs of an intervention and is also often applied to treatments for which the evidence base is still evolving. So what can *BMJ Clinical Evidence* tell us about the state of our current knowledge? Figure 1 illustrates what percentage of around 3000 treatments included in *BMJ Clinical Evidence* fall into each category.

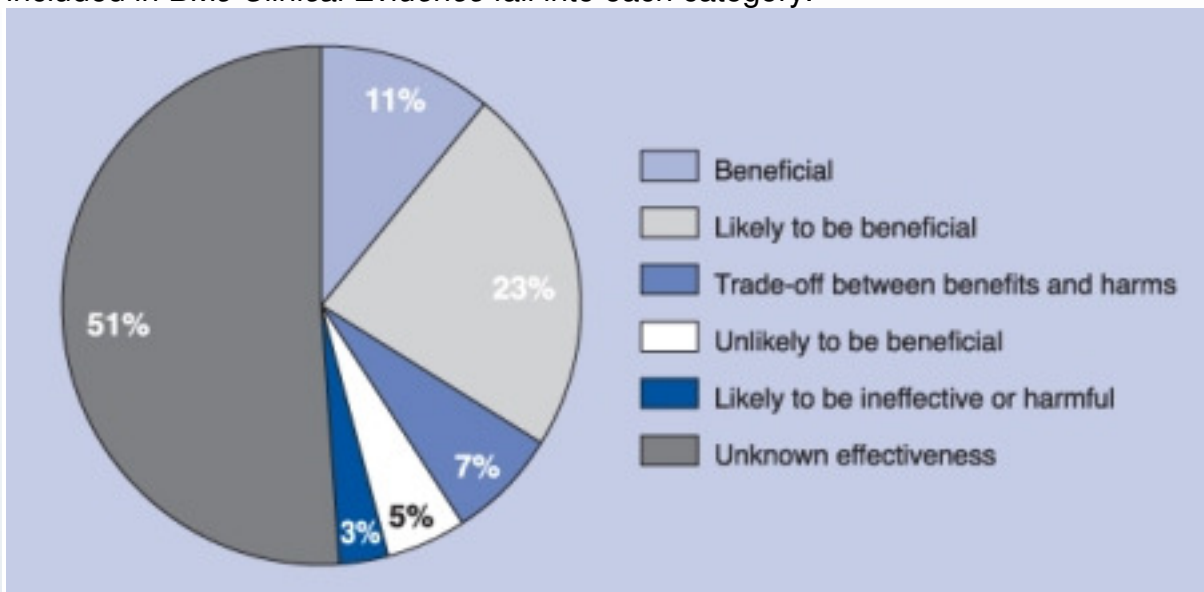


Figure 1.

We have to be very careful when assessing some medicines which, in the real world, may evolve from one category to another and all levels of evidence must be considered.

The KCE methodology is only considering the highest level of evidence and even higher using uncommon methodology: a review of reviews. Normally all levels are considered for the evaluation of clinical efficacy in medicine. Knowing these limitations of EBM's highest level, conclusions of the evaluation using only this methodology must be made with caution.



KCE procedure for selection and rejection of publications

It is impossible to evaluate the validity of the KCE selection and rejection procedure. The report gives only a flow chart of literature search and selection, resulting in the selection of 26 papers. Reasons for rejection are not explained in detail and not even numbered correctly, as example 56 publications are rejected based on full text evaluation but only for 37 a reason for rejection is given: intervention 10; outcome 3; design 24. The report is therefore not adequately systematic or transparent in its approach.

The RWG decided to reproduce the same exercise using the methodology described by the KCE.

RWG comments on selection and rejection of papers

Part 1

In the **first part** of this exercise, comparing the reviews of the KCE report with those listed on the website of the Faculty of Homeopathy (UK), we have identify 19 reviews (mostly systematic reviews) that are missing. Of these 19 missing reviews, 11 are positive, 4 are non-conclusive and 4 are negative. Fifteen of the 19 were published on or after 2000. So it appears clearly that the KCE authors used an inferior literature search strategy.

In table 1 (p.16) - Assessment of selected studies - the 27 included papers are listed. The Shang 2005 paper (1) has been added even if irrelevant for the chosen methodology and containing demonstrable bias (2, 3).

They are also some serious errors of inclusion (or expressed results) in the 26 selected publications.

Several papers are wrongly included or quoted:

Ref. 32 in KCE report about nocturnal enuresis in children (4) did not report any RCTs in homeopathy; as such it is wrong to write that that they found no evidence that homeopathy is effective: homeopathy has not been analyzed at all.

Ref 31 in KCE report about homeopathy for dementia (5) did not report any RCTs in homeopathy; as such it is wrong to write that that they found no evidence that homeopathy is effective: homeopathy has not been analyzed at all.

Ref 39 in KCE report about wandering in dementia (6) did not report any RCTs in homeopathy; as such it is wrong to write that that they found no evidence that homeopathy is effective: homeopathy has not been analyzed at all.

About **fibromyalgia**, at page 18 of KCE report, the KCE conclusions are incomplete and therefore misleading:



Langhorst et al. (7) concluded that homeopathy could be recommended at least for a limited period of time.

Baranowsky J et al. (8) report, positive results were noted for homeopathy.

De Silva V et al. (9) concluded that even if the homeopathic studies were small each reported an improvement in pain.

Perry et al. 2010 (10) reports all four RCTs. De Silva et al. 2010 (9) report on three trials (Fischer et al. 1986, Fischer et al. 1989 and Bell et al. 2004), Langhorst et al. 2008 (7) doesn't report on Fischer et al. 1986. Baranowsky et al. 2009 (8) on Bell et al. 2004 and Holdcraft et al. 2003 (11) only report Fischer et al. 1989.

About **cancer related symptoms**: at page 17 of the KCE report, pooling the assessment of efficacy of ointment preparations aimed at local effect and oromucosal preparations aimed at a global effect is analogous to pooling the effect of cough preparations and antibiotics in examining the efficacy of bronchitis treatments. Conclusions from such analysis should be differentiated, not pooled.

First conclusion for cancer related symptoms (KCE ref.46): there is preliminary data supporting the efficacy of topical homeopathic preparations; further research is required.

Second pooled conclusions for cancer related symptoms (KCE ref.36-46): there is no convincing evidence for efficacy of homeopathic medicines for adverse effects of cancer treatments; further research is required.

About **depression**: the KCE report reported no RCT for this topic, referring to Pilkington et al. 2005 (12). This is a wrong conclusion: 2 RCTs are included; the third reported on chronic fatigue, and authors concluded that evidence for the effectiveness of homeopathy in depression is limited because of a lack of high-quality clinical trials or inappropriate control.

Only 18 diagnoses are commented on in detail in the KCE report (p.16-18), some without available data, as explained before. However, the reference used for "Third trimester cervical ripening or induction of labour" is not the reference in the list: it is an old report from the same author. The reference used for "Chronic fatigue" is only an abstract of the listed study.

After this first scrutiny we could already conclude that the KCE literature review of reviews is objectively questionable. We identified several major errors of inclusion/exclusion procedure and of results interpretation. A number of included diagnoses have never been investigated in RCTs, justifying the RWG's conclusion: more research is needed and must be supported.



Part 2

In the **second part** of this exercise, the RWG carried out its own systematic review of systematic reviews of RCTs in homeopathy.

Methodology

We performed a systematic review of systematic reviews. Systematic reviews and meta-analyses were searched in Medline, Embase and Cochrane Database of Systematic Reviews, search date up to and including May 2011. Search term used was homeopath* with limits on 'review, human, English, French, German'. Hand search has been performed for the following sites: <http://www.britishhomeopathic.org>, <http://www.homresearch.org/Publikationen.html>, <http://www.facultyofhomeopathy.org/research/>.

Reference lists have been scanned and expert knowledge has been added.

Inclusion criteria: search date of reviews after 2000, reviews that report on a specific condition, reviews with clear reporting of outcome measures and results

Exclusion criteria: narrative reviews, reviews on specific homeopathic medication (arnica), reviews without clear methodology.

There is evidence for the efficacy of homeopathic remedies in single conditions.

There is convincing evidence for the efficacy of Aconitum in post-operative agitation in children (13-15).

There is convincing evidence of efficacy of Belladonna 7cH and X-ray 15cH (Balzarini 2000) (16) and topical calendula (Pommier 2004) (17) for the treatment of radiodermatitis and for Traumeel S for the treatment of chemotherapy- induced stomatitis (Oberbaum 2001) (16-18).

There is evidence for the efficacy of homeopathy for diarrhoea in childhood. This is confirmed by two meta-analyses (18-20).

There is strong evidence that homeopathy works for upper respiratory tract infections (URTI) (1, 18, 21, 22).

Ulman et al. (23) reported that homeopathic medicine may play a useful role as an adjunctive and/or alternative therapy for HIV.

Oscillococcinum can treat influenza-like symptoms (24).

Some evidence exists to support the superiority of homeopathic remedies over placebo for treating osteoarthritis and rheumatoid arthritis (25-27).

The evidence for the efficacy of homeopathy in fibromyalgia is based on four RCTs which all reported positive results (7-10).

When taking into account the evidence for upper respiratory tract infections, allergic rhinitis and allergic conditions, we conclude that there is a positive overall result in favour of homeopathy for these three conditions.(18, 21, 28).



Evidence of homeopathic efficacy from before 2000 in single conditions:

Isopathic nosodes were different from placebo on both subjective and objective measures for allergic conditions (29).

The available evidence is positive for post-operative ileus (1, 30, 31).

Galphimia glauca is statistically significantly more effective than placebo for seasonal allergy (30, 32).

Possible possible evidence in single conditions:

Insomnia (33, 34), chronic fatigue syndrome (35), low back pain (36), depression (12), ADHD (15, 37).

Conclusion of the review of reviews:

It is clear that the search to highest clinical level of evidence for homeopathy reported by the KCE report is of poor quality. Its conclusions are clearly questionable:

- 1) reviews are included that didn't include any clinical trial on homeopathy (4-6)
- 2) references are wrongly used and do not concern the trials included (6, 38)
- 3) the content of the reviews is poorly reported and contains a number of errors (4, 6, 12, 14, 15, 39-42)
- 4) references are not correctly cited (15, 33-35, 41, 43, 44)
- 5) authors' conclusions are not correctly reported (35)
- 6) reviews are not included by KCE (10, 11, 18, 21, 23, 26, 28, 45-49). We do not know if these reviews were not found by the KCE authors or if they were excluded for some reason
- 7) the exclusion of reviews with search date before 2000 has led to a misrepresentation of the evidence overall

We found clinical evidence in favour of efficacy of homeopathic medicine for several conditions. Of course more research is needed for all conditions not yet or poorly investigated. This research, plus replication of existing RCTs, must be encouraged and supported.

We found similar conclusions in a previous published paper by Mathie (50). The author concluded *that **positive** systematic reviews exist for childhood diarrhoea, seasonal allergic rhinitis (placebo controlled and also other control groups), vertigo, post operative ileus; **not conclusive** systematic reviews for headache/migraine,*



*induction of labour, anxiety, depression, chronic asthma, osteoarthritis, influenza and **negative** systematic reviews for prevention of headache/migraine, prevention of influenza, ADHD and delayed-onset muscles soreness.*

The author concluded also that these results *“for any given medical condition need to be confirmed or refuted by additional original research, which should focus explicitly on the efficacy or effectiveness of a well-defined homeopathic intervention for a given medical condition or – perhaps more relevantly for homeopathy – for a given symptom picture”*.

At least, even for this highest level of evidence, **it is factually incorrect to state that no proof of efficacy exists for any medical condition for which a systematic review is available.**

To evaluate efficacy of a medicine all available data from all levels of evidence must be pooled. A very broad spectrum of full and accurate results exists in which homeopathic treatments have been compared with other approaches. The best examples are the surveys organized systematically by several health services in Europe.

In these studies, the improvements are statistically and clinically significant, especially for asthma in children, headache, cancer patients, allergies, general problems, intestinal disorders, anxiety disorder, depression and skin problems, respiratory problems, diabetic poly-neuropathy, chronic problems in the ear, nose and throat area, as for example sinusitis, problems during pregnancy. These are also the most common diagnoses in general practice. (51-53)

In the LMHI/ECH booklet “Scientific Framework of Homeopathy” all references for all levels are described. Pooling all data together (also about cost-benefit studies) the conclusion would be that for allergic conditions homeopathic medicine is a first choice in first-line medicine.

About clinical efficacy of homeopathy the RWG concludes that:

- KCE’s chosen methodology can be strongly questioned regarding a global EBM evaluation procedure.
- Very serious errors are identified regarding the application of the inclusion and exclusion procedure.
- Key message of KCE about clinical efficacy is not appropriate and would be more appropriately stated: *“Even considering only the highest level of evidence, there is some proof of efficacy of homeopathic medicines for several diagnoses (page 8). Confirmation of these findings is needed. Pooling all available literature, from all levels of evidence, is recommended for further assessment.”*
- Efficacy of homeopathy for many diagnoses has never been investigated. More research is needed and must be supported.



Other parts of the KCE report

The most interesting parts of the KCE report (and most developed) are certainly the surveys on the use of homeopathy in Belgium, on the practice and the study of organisational and legal aspects of homeopathy in Belgium.

It contains very interesting information that could serve for comparison with other countries in the world. Remember that some conclusions of this survey can be questioned for the use of non-representative sample of homeopathy users (p.25). The same problem exists for the practice (p.56); this problem is well addressed in the discussion about limitations of the surveys (p.95).

About legal aspects, the RWG appreciated greatly the explanations about registration of homeopathic medicines (p.72) in Belgium following European rules.

The RWG considers that clarifications are needed about the legally guaranteed freedom of prescription by a medical doctor and delivery of homeopathic medicine by a pharmacist opposed to the compulsory limitation for a medical doctor to EBM interventions. The consideration of the global EBM evaluation system, as explained before, is certainly the key to the answer. Other countries in the world have included homeopathy officially in medical practice, the last one in Europe being Spain see www.homeopathyeurope.org

The RWG was disappointed about the fact that several important themes around homeopathy are not considered or studied in detail in the KCE report. These missing parts are lowering or even questioning the power or validity of the conclusions of the KCE report.

RWG comments of missing parts and wrong statements

The homeopathic remedy specificity (p.ii) is not considered in the KCE report, which contains archaic definitions and wording regarding homeopathy.

Homeopathy is modern medicine and the authors of the KCE report have not adapted their terminology to reflect modern usage. On www.lmhi.org the definition of homeopathic medicines is available. Each word of this definition is explained in detail; this definition has been submitted to a worldwide discussion and has been accepted in LMHI GA of 2010 in USA:

“A homeopathic remedy is prepared from a stock/raw material described in a homeopathic monograph/source, following a homeopathic method and administered to a living being according to the principle of “similia similibus curentur”. It has a potential to support changes in the state of health of this living being. When such changes indeed happen and lead to an improvement in the state of health/full healing of a disease with recovery of the state of health, homeopathic medicines act as remedies.”

Other definitions of homeopathic terminology are available on

<http://www.homeopathyeurope.org/downloads/homeothesaurusmulti.pdf>



The homeopathic medicines are also officially allowed and registered medications in most European countries. The rules of the origin and the quality of the stocks and the processes of the preparation of the homeopathic remedies are given in the pharmacopoeias and in the “Working Party on „Control of Medicines and Inspections”. Guide to Good Manufacturing Practice, see:

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2001L0083:20070126:EN:PDF>

The European pharmaceutical homeopathic medicinal product definition is:
“Any medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the Member States. A homeopathic medicinal product may contain a number of principles.”

Economic parameters in surveys are eliminated as selection criteria about efficacy and not considered further in the KCE report. These are important elements for decision-making about reimbursements and population health costs. Without a study of these parameters recommendations about reimbursement are questionable. As example see: Peter Kooreman, Erik Baars: Patients Whose GP Knows Complementary Medicine Have Lower Costs and Live Longer, May 31. 2010. in: www.members.ziggo.nl

Fundamental research on mechanisms (p.20) is referred to as “*not for consideration*” but is nevertheless commented (p.12) on, using the “Benveniste Memory of Water affair in Nature” as example. The KCE report says that this model has not been reproduced. This is not true. This specific research model (technically improved) has been reproduced several times in recent years by different and independent laboratories. (54-58) Other models with positive results were published also in international peer reviewed journals, as for example the model with high diluted thymuline and thyroxine. Int J Immunotherapy 1987 ;3 :191-200 (**Thymulin** in mice, Bastide M,), J Vet & Human Toxicol 1995 ;37(3) :259-260/ Homeopathy 2008;97:3-9 (**Thyroxine**, Endler PC,),

The KCE did not analyse **the homeopathic market** (selling and delivery of remedies by companies and pharmacies in Belgium) saying that it was not possible, the same for the use of allopathic concomitants prescribed by medically qualified homeopaths or used by patients (p.24; p.100). These figures are important to evaluate the real use of homeopathy in the Belgian population. Without the analysis of these facts their recommendations about reimbursements of homeopathic drugs and practice are invalid.

Self medication / Role of pharmacists / Use of homeopathy by conventional medical practitioners (p.95) have not been considered (in France it has been shown that it are important phenomenon’s). These aspects are important to differentiate the role of the prescribers and the OTC approach.



The role and facts from the **homeopathic industry** is another topic that has influence on many aspects of homeopathy such as registration of homeopathic medicines, research, prices of medicines etc. Without a clear analysis of these facts it is impossible to advice correctly on homeopathy.

At page 100 the KCE report states that the **risk of delayed diagnosis** has not been considered. But at page 18 it has well been considered and only some anecdotal evidence for delayed diagnosis (3 cases) were found.

The KCE report states that the **prescription of concomitant conventional drugs** such as antibiotics has not been analysed (p.105). This information is needed to allow good recommendations about homeopathic medical practice.

In the recommendations (p.vii) the use of homeopathic medicines is considered as very **safe due to the dilution** process. But at page 56 we found that 63 % of homeopathic medicines are prescribed in Belgium in “low” dilution. Even if the registration process, using the concept of “first safe dilution for each medicine” (p.72), can be a key approach to avoid the risk of homeopathic use of lowest dilutions (high concentrations such as MT and D dilutions) the conclusion must be that homeopathic medicines are mostly prescribed in Belgium in low dilutions. A market survey would be a better tool for such evaluation.

The dilution process is not a law but a specific preparation method as explained in the LMHI definition (see above). Safety of homeopathy comes also from a Good Medical and Homeopathic Education and a Good Medical and Homeopathic Practice. It has been demonstrated that a unique intake of a high diluted homeopathic medicine is not life threatening (remember “collective suicides”). The use by a patient suffering of chronic disease of repeated high dilutions of a homeopathic medicine can be considered as a small risk for side effects. Provings using high diluted homeopathic medicines in healthy volunteers are the second step to approach pathogenetic symptoms. It is a very long tradition and it has been experienced by many generations. Traditional homeopathic sources and literature all indicate that there is a very low risk for serious adverse reactions in provings on healthy volunteers, on the condition that doses are discontinued whenever clear reactions occur.

Agrohomeopathy and Homeopathic veterinary practice were not considered in the KCE report. This is an important shortcoming, preventing a sound, objective and complete evaluation of efficacy of homeopathy.



About missing parts and wrong statements the RWG concludes that:

- The KCE report contains interesting sociologic surveys but terminology is not adapted to modern homeopathic practice and wording.
- Many missing parts lower the value of the recommendations of the KCE about homeopathic practice, safety and reimbursement of homeopathic practice and medicines.
- The KCE statement about efficacy of homeopathy is also questionable considering the absence of an evaluation of homeopathic veterinary practice, agro-homeopathy and fundamental research in homeopathy.

REPORT Supplement VERIFICATION

REVIEW OF REVIEW

of KCE Randomized Controlled Clinical Trials in specified diagnoses

**Research working group (RWG) of the
LIGA MEDICORUM HOMOEOPATHICA INTERNATIONALIS (LMHI)**

about

Clinical Efficacy of Homeopathy

This complementary report is a response to the Belgian KCE report
evaluating clinical efficacy of homeopathy



General remarks:

- 1) This review is directed to an evaluation of RCTs in each defined diagnosis where such research has been performed for homeopathy. It is limited to this highest level of evidence that measures efficacy of a medical intervention. All other designs are excluded.
- 2) The impact of homeopathy on the health of patients (effectiveness), the reasons for which they are visiting homeopaths, and which patients are visiting homeopaths can be evaluated by cohort studies or socio-demographic studies.

METHODOLOGY

We performed a systematic review of systematic reviews. Systematic reviews and meta-analyses were searched in Medline, Embase and Cochrane Database of Systematic Reviews, search date till June 2011. Search term used was homeopath* with limits on 'review, human, English, French, German'. Hand search has been performed for the following sites: <http://www.britishhomeopathic.org>, <http://www.homresearch.org/Publikationen.html>, <http://www.facultyofhomeopathy.org/research/>. Reference lists has been scanned and expert knowledge has been added.

Inclusion criteria: search date of reviews after 2000, reviews that report on a specific condition, reviews with clear reporting of outcome measures and results

Exclusion criteria: Narrative reviews, reviews on specific homeopathic medication, reviews without clear methodology.



EVIDENCE TABLES

1) Insomnia (33, 34)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Insomnia	Individualised homeopathic medicine (agreed by 2 homeopaths) then placebo.	4 (34)	Carlini et al. 1987	No consistent differences between patients starting on intervention or placebo		The limited evidence available does not demonstrate a statistically significant effect of homeopathic medicines for insomnia treatment.	See below concerning the note of Sarris 2010(38)
	Formulaic homeopathic medicines: Homeogene-46a or Sedatif-PC vs placebo		Cialdella et al. 2001	no significant difference between groups.			
	Formulaic homeopathic medicine Requesan vs placebo		Wolf 1992	difference between groups not significant			
	Formulaic homeopathic medicine: Coffea cruda 200c vs placebo		Kolia-Adam et al. 2008	no significant difference between groups			
	Individualized homeopathy versus placebo (33)	1	Naudé 2010	statistically significant result (p < 0.036) hours sleep, summary scores (p < 0.001)		We would like to see further sufficiently powered and well-conducted RCTs of homeopathy for insomnia to assess whether the results of Naudé et al. can be replicated.	

One small study with 30 patients receiving individualized homeopathy is statistically and clinically significant (increased from 35 to 41 hours sleep per week in the treatment group). This trial needs replication. The reference Sarris 2010 (38) marked by the KCE on the quality of the RCTs did not concern the above mentioned RCTs. The only described RCT on homeopathy was excluded because it handled jetlag, not insomnia.



2) LOW BACK PAIN(36)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Low back pain	homeopathic gel (Spiroflor SRL) vs Cremor Capsici Compositus (CCC)	1	Stam et al 2001	SRL and CCC are equally effective in the treatment of LBP; however, SRL has a lower risk of adverse effects	1 RCT of high quality	low number of trials (one trial) investigating homeopathy prevents definite conclusions being drawn	

Spiroflor SRL is as effective for treatment of low back pain as cremor capsici compositus (CCC) (product containing salicylate).

3) Induction of labour (43)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Induction of labour	homeopathic vs placebo	2	Beer 1999 Dorfman 1987	no differences in any primary or secondary outcome between the treatment and control group	Quality low lacked clinically meaningful outcomes	There is insufficient evidence to recommend the use of homeopathy as a method of induction of labour	Reference is wrongly dated 2001, should be 2003

There is insufficient evidence to recommend the use of homeopathy as a method of induction of labour.



4) Chronic fatigue syndrome (35)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Chronic fatigue	Individualized homeopathy vs placebo	2	Awdry 1996	Greater improvement with treatment than in control group (no figures presented)		Homeopathic therapies were evaluated in two RCTs, one of poor quality and one of good quality. Some positive effects of homeopathy were seen in the better quality trial.	Authors conclusion not added
			Weatherley-Jones 2004	<i>Fatigue, functional limitations:</i> significant differences in favour of treatment group for fatigue (p=0.04) and some physical dimensions of the Functional Limitations Profile (p value not reported)			Wrong reference (only abstract used)

The two trials report benefit from individualized homeopathic treatment on symptoms of chronic fatigue syndrome.

5) Dementia (5)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
dementia	Aluminium 30 C	0			One excluded study (Davies 1988)	In view of the absence of evidence, it is not possible to comment on the use of homeopathy in treating dementia.	Authors Conclusion wrongly reported: no evidence found

There is currently no evidence in the form of controlled clinical trials to either support or oppose the use of homeopathy for treating dementia. In view of the absence of evidence, it is not possible to comment on the use of homeopathy in treating dementia.

6) Wandering in dementia (6)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Wandering in dementia		0	No studies found				Authors Conclusion wrongly reported: no evidence found

There is currently no evidence in the form of controlled clinical trials to either support or oppose the use of homeopathy for treating wandering in dementia. In view of the absence of evidence, it is not possible to comment on the use of homeopathy in treating wandering in dementia.



7) Chronic asthma (39)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Asthma	Individualized versus placebo	1	White et al.(2003)	No changes of QOL, small not significant improvement of symptoms in verum group	trials of variable quality	There is not enough evidence to reliably assess the possible role of homeopathy in asthma	Wrongly 5 RCT's mentioned
Allergic asthma	Homeopathic complex Engystol-N versus placebo	5	Matusiewicz 1995,	Clinical improvement only in verum group			
	Homeopathic complex Asthma H Inj. Plfugerplex (subcutaneously)		Matusiewicz et al. (1999)	Slight decrease of conventional medication and infections; no change in spirometric tests			
	Dust mite homeopathy vs placebo		Lewith et al 2002	No difference between active and placebo in FEV1, PEF, symptoms, use of b2-agonists, and asthma score			
	Isopathy vs placebo		Reilly 1994	daily 100 mm visual analogue scale improved by 7.2 (standard deviation 10.6) mm in the treatment group while there was a deterioration by 7.8 (10.8) mm in the placebo group. The difference between the groups is highly significant (p = 0.003). No significant difference was observed for PEF.			
	Blatta officinalis C6) vs placebo		Freitas 1995	No significant difference was reported between the groups in terms of intensity, frequency and duration of exacerbations.			

There is not enough evidence to reliably assess the possible role of homeopathy in asthma.



8) Enuresis (4)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
enuresis		0			There were no randomised controlled trials of homeopathy	There were no trials including homeopathy	Authors Conclusion wrongly reported: no evidence found

There is currently no evidence in the form of controlled clinical trials to either support or oppose the use of homeopathy for treating enuresis. In view of the absence of evidence, it is not possible to comment on the use of homeopathy in treating enuresis.

9) Depression (12)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
depression	Non-individualized Homeopathy L72 vs diazepam	1	Heulluy 1985	L72 as effective as diazepam on all measures (thymo-effective, somatic and objective parameters)		Evidence for the effectiveness of homeopathy in depression is limited because of a lack of high-quality clinical trials	Wrongly 0 RCT's mentioned Authors conclusions are wrongly reported
	Homeopathy vs fluoxetine	1	Katz et al. 2005		Not reported due to low numbers		

Pilkington found three RCTs of low quality:

1. inappropriate comparator (diazepam) for depression
 2. small number of included patients N=11 (comparator fluoxetine)
 3. the third trial looked at depression associated with chronic fatigue syndrome rather than depression per se; it has therefore been excluded.
- Appropriate methods for design, diagnosis, outcome and recruitment are necessary when re-conducting these trials. Given the limited availability of RCTs on depression at present, it is not possible to draw conclusions about the efficacy of homeopathy in depression.



10) Anxiety (14)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Anxiety in children	Aconitum versus placebo	1	Alibeu and Jobert 1990	'Effective with 95% good results'	95% good results were reported' many of the methodological details, such as randomisation, allocation concealment and blinding are unclear	On the basis of this review it is not possible to draw firm conclusions on the efficacy or effectiveness of homeopathy for anxiety.	Authors conclusions are wrongly reported
Anxiety in adults	Argentum nitricum 12x vs placebo	7	Baker 2003	No significant difference	Argentum nitricum 12x vs placebo		
	Individualised homeopathy vs placebo		Bonne 2003	No significant difference between groups	Individualised homeopathy vs placebo		
	Non-individualised L72 vs lorazepam		Heulluy 1985	'L72 as effective as diazepam on all measures'	Non- individualised L72 vs lorazepam		
	Anti-Anxiety, vs placebo		McCutcheon 1996	No significant differences in STAI or pulse rate between groups Significantly less sleep loss in homeopathy group	Anti-Anxiety, vs placebo		
	Argentum nitricum 12x vs placebo		Stanton 1981	Homeopathic preparation significantly improved test anxiety compared with placebo	Argentum nitricum 12x vs placebo		
	Individualised prescribing vs placebo		Thompson 2005	No difference between groups	Individualised prescribing vs placebo		
	Lithium Microso vs diazepam		Hariveau 1995	outcomes: not mentioned	Lithium Microso vs diazepam		

There is evidence for the efficacy of Aconitum in post-operative agitation in children.



11) Cancer related symptoms (16, 17, 59)

Kassab et al. report on eight trials (Balzarini 2000, Jacobs 2005, Kulkarni 1988, Oberbaum 2001, Pommier 2004, Thompson 2005, Bourgois 1984, Daub 2005) which is three more trials (Pommier 2004, Bourgois 1984, Daub 2005) than Millazzo et al., who report only on five RCTs (Oberbaum 1998 is a non-randomized trial). Rada et al. reports only on menopausal symptoms, hot flushes in breast cancer patients (Jacobs 2005, Thompson 2005).

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
adverse effects of radiotherapy/ radiodermatitis	Cobaltum 30 Causticum 30	1	Kulkarni 1988	"about 30%" reduction in the degree of reactions in both groups taking homeopathic medicines compared with placebo		Two other studies reported positive results, although the risk of bias was unclear	
	Belladonna 7cH and X-ray 15cH	1	Balzarini 2000	a statistically significant reduction in total severity during recovery for the group treated with homeopathy (P = 0.05)			
	topical calendula preparation vs trolamine	1	Pommier 2004	the occurrence of acute dermatitis grade two or higher was significantly lower (41% versus 63% P < 0.001) with the use of calendula than with trolamine			
adverse effects of chemotherapy/ protect venous function	Arnica 5c or placebo	1	Bourgois 1984	no statistically significant differences between active and placebo groups		superiority of topical calendula over trolamine (a topical agent not containing corticosteroids) for prevention of radiotherapy-induced dermatitis, and another with 32 participants demonstrated superiority of Traumeel S (a proprietary complex homeopathic medicine) over placebo as a mouthwash for chemotherapy-induced stomatitis	
adverse effects of chemotherapy/ stomatitis	TraumeelS	1	Oberbaum 2001	statistically significant benefits in both comparisons for the group receiving homeopathy			
adverse effects of chemotherapy/ antiemesis	Homeopathy vs placebo	1	Daub 2005	no significant difference between the two groups			
menopausal symptoms	Homeopathy vs placebo	1	Jacobs 2005	no significant differences in the hot flush severity score between the groups			
	Homeopathy vs placebo	1	Thompson 2005	no statistically significant differences between groups			

There is convincing proof of efficacy of topical Calendula (Pommier 2004) for the treatment of radiodermatitis and for Traumeel S for the treatment of chemotherapy-induced stomatitis (Oberbaum 2001). Belladonna 7cH and X-ray 15cH (Balzarini 2000) and Cobaltum 30 and Causticum 30 may be effective for the treatment of radiodermatitis, although the risk of bias is unclear in these studies.



12) Childhood ailments (15, 19, 37)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Adenoid vegetation	Homeopathy vs placebo	2	Feuchter et al. 2001 Furuta et al. 2003	No intergroup difference No intergroup difference			
ADHD	Homeopathy vs placebo	3	Strauss et al. 2000	Intergroup difference for PSQ (Connors Parent Symptom Questionnaire) ($P=.01$)	The forms of homeopathy evaluated to date do not suggest significant treatment effects for the global symptoms, core symptoms of inattention, hyperactivity or impulsivity, or related outcomes such as anxiety in Attention Deficit/Hyperactivity Disorder.(37)		
			Jacobs et al. 2005 Frei et al. 2005	No intergroup difference Intergroup difference for Connors Global index ($p<0.048$)			
		1	Lamont et al. 1997	Improvement in an unpublished five- point scale of change in hyperactivity			
asthma	Homeopathy vs placebo	2	Freitas et al. 1995	No intergroup differences			
			White et al. 2003	No intergroup differences			
otitis	Individualized homeopathy vs placebo		Jacobs 2001	intergroup differences for symptom scores ($P<.05$), no intergroup differences for treatment failures, ear effusion			
conjunctivitis	Homeopathy vs placebo	1	Mokkapatti. 1992	No intergroup differences			
diarrhoea	Individualized homeopathy vs placebo		Jacobs. et al. 1993	No intergroup differences (underpowered N=34)			
			Jacobs 1994	intergroup differences for both outcome measures ($P=.048$ and $P<.05$, respectively)			
			Jacobs 2000	Intergroup differences for both outcome measures ($P=.04$ and $P=.02$, respectively)			
	Meta-analyse	3	Jacobs 2003 (19)	The meta-analysis shows a consistent effect-size difference of 0.66 day ($P < 0.008$).			
Post-operative agitation	Aconitum vs placebo	1	Alibeu 1990	Intergroup difference ($P<.05$)			
URTI (Upper Respiratory Tract Infection)	Homeopathy vs placebo	2	De Lange et al. 1994	No intergroup differences			
			Steinsbekk et al. 2005	No intergroup differences			
Warts	Ind. homeopathy vs placebo	1	Kainz et al. 1996	No intergroup differences			



Altunc et al. report on different diagnoses in children. Jacobs et al 2003 has done a meta-analysis of the three included RCTs on diarrhoea. Coulter 2007 added a fourth RCT on ADHD (Lamont 1997)

There is no convincing evidence for the efficacy of homeopathy in children for adenoid vegetations, asthma, conjunctivitis, upper respiratory tract infections and warts.

There is currently little evidence for the efficacy of homeopathy for the treatment of ADHD. Development of optimal treatment protocols is recommended prior to further RCTs being undertaken.

A single RCT (N=75) assessed patients with acute otitis media and reported a statistically significant decrease in symptom scores ($p < 0,05$) compared with placebo as recorded by parent diaries. These data require independent replication.

There is evidence for the efficacy of homeopathy for diarrhoea in childhood. A meta-analysis, done by Jacobs et al.(19) reported a consistent difference of 0,66 days between the two treatment groups, which is statistically highly significant ($p < 0,008$).

There is evidence for the efficacy of Aconitum in post-operative agitation in children.



13) *Fibromyalgia (7-9, 11)*

Perry et al. 2010 reports all four RCTs. De Silva et al. 2010 report on three trials (Fischer et al. 1986, Fischer et al. 1989 and Bell et al. 2004), Langhorst et al. 2008 does not report on Fischer et al. 1986. Baranowsky et al. 2009 on Bell et al. 2004 and Holdcraft et al. 2003 only report Fischer et al. 1989.

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Fibromyalgia	Rhus toxicodendron 6c vs placebo	1	Fischer et al. 1989	Significant improvement in tenderness (P < 0.005), pain and sleep was observed (P < 0.005)		Within a multicomponent therapy setting, homeopathy can be recommended for a limited period of time.(7)	Wrongly reported as: Very low quality evidence
	Arnica, Bryonia, Rhus toxicodendron 6c vs placebo	1	Fischer et al. 1986	Significant improvement in pain (P<0.05) and sleep (P<0.05)		limited evidence for homeopathy(11) The homeopathy studies were small, but each reported an improvement in pain. (9)	
	Individualized homeopathy vs placebo	1	Bell et al. 2004	Significant improvement in active group in TPC and TP pain on palpation, Appraisal of FM scores, global health ratings and helpfulness of treatment as compared to placebo group.		These results show homeopathy to be a promising option in the treatment of fibromyalgia. Yet, further clinical trials are needed to confirm these findings with bigger sample sizes and follow-ups and to create an eventual evidence- based basis for homeopathic treatment in fibromyalgia (8)	
		1	Relton et al. 2009	Change in outcome scores: Significant greater reduction in the FIQ total score in the homeopathic care group -6.53 (15.03) compared to usual care 1.74 (12.85) p<0.01. N/s difference in FIQ pain score.		the findings of the four existing RCTs all favour homeopathy over controls. Yet none of the studies is sufficiently rigorous to provide a definitive answer. Future studies should minimise bias more effectively than did the trials available so far.(10)	

Four RCTs have been done with a different homeopathic treatment, all reporting positive results. These results show homeopathy to be a promising option in the treatment of fibromyalgia. Yet, further clinical trials are needed to confirm these findings with bigger sample sizes and follow-ups and to create a fully evidence-based approach for homeopathic treatment in fibromyalgia.



14) HIV (23, 60)

Mills et al. 2005 report on Struwe et al. 1993 and Rastogi et al., 1999. Ullman 2003 report also on Rastogi et al., 1999 and add the trial of Brewitt et al., 2002.

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
CD4 Body fat symptom distress	Homeopathy vs placebo	1	Struwe et al. 1993		Small sample size, concerns about conduct of trial, flaws in analysis	Evidence inconclusive (60)	
	Individualized homeopathy	1	Rastogi et al., 1999	Statistically significant change in CD4 T-lymphocytes counts ($p = 0.008$). There was also a statistically significant elevation of CD8 T-lymphocytes ($p = 0.04$).		Homeopathic medicine may play a useful role as an adjunctive and/or alternative therapy (23)	
CD4 counts QoL	homeopathic growth factors vs placebo	1	Brewitt et al., 2002	Statistically significant change in CD4 T-lymphocytes counts ($p = 0.03$) A statistically significant improvement was found in subjects using the combination of homeopathic growth factors compared to placebo			

15) Chronic venous insufficiency (40)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
venous filling time, leg volume and subjective symptoms	complex homeopathic remedy vs placebo	1	Ernst et al. 1990	the experimental group had significantly better outcomes in terms of venous filling time, leg volume and subjective symptoms	No independent replication of this trial has so far been reported.		No conclusions were drawn by the authors concerning homeopathy

Ernst et al. found inconclusive evidence for an effect on venous filling time, leg volume and subjective symptoms based on one small trial; needs replication.



16) Premenstrual syndrome (41)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Premenstrual syndrome	Homeopathy vs placebo	1	Chapman 1994	rigorously designed the selection criteria were so strict that only 10 of the 205 women screened actually participated. The lack of statistical power renders the results inconclusive		The current evidence for homeopathy is not particularly promising, with trial results indicating little more than a placebo response	The review is based on Chapman 1994. Lepaisant et al.1995 was excluded. The publication date is 2001 and not 2000
	Five commonly used homeopathic medications	1	Yakir et al. 2001 (61)	Difference in mean MDQ scores between active treatment, and placebo (P= 0.057) Improvement >30% was observed in 90% of patients receiving active treatment and 37.5% receiving placebo (P 1/4 0.048)	Small (N=20) pilot study	The use of symptom clusters in this trial may offer a novel approach that will facilitate clinical trials in homeopathy. Further research is in progress.	

Stevinson et al. found no conclusive evidence, based on one underpowered RCT. The pilot study of Yakir et al.(61) was not included, results are positive, replication needed.



17) *Allergic rhinitis (45, 62)*

Bellavite et al.(28) include four more trials on allergy, namely:

- Aabel et al. 2001, which confirms that Birch pollen 30 C is not suitable to treating allergic rhinitis.
- Two more studies with Galphimia (Wiesenauer and Ludtke (1987), (1995). Passalacqua et al. 2006 report only the first negative trial done with Galphimia. A meta-analysis of all 7 RCTs including the first one, done with Galphimia (Lüdtke 1997 (63)) shows a significant superiority over placebo. This is confirmed by the meta-analysis done by Linde 1997 (30) and Jonas 2003 (64).
- A fourth study (Hardy (1984) used a homeopathic preparation of house dust.

Taylor et al. 2000 report on a trial with 50 patients and the pooled analyses of three other trials on a total of 253 randomised patients. These findings have not been reported by Passalacqua et al. 2006.

There is evidence that homeopathic preparations of house dust (Hardy 1984), 30c dilution grass (Reilly et al 1986), Nasal Luffa compositum Heel (Weiser et al 1999), homeopathic grass, trees, weeds mix (Kim et al 2005) and 30c dilution of allergens (Reilly et al 1986) can be useful for the relief of symptoms of allergic rhinitis . There is strong evidence that Galphimia (Lüdtke 1997) and 30c dilution of various allergens (Taylor 2000) is effective for allergic rhinitis.



Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Allergic rhinitis	Birch 30c vs placebo	1	Aabel et al 2000	No effect on symptoms		Some positive results were described in rhinitis with homeopathy in good-quality trials, but an equal number of negative studies counterbalance the positive ones. Therefore it is not possible to provide evidence-based recommendations for the use of homeopathy to treat allergic rhinitis, and further randomized controlled trials are needed. (45, 62)	
		1	Aabel et al 2000	No effect on symptoms			
		1	Aabel (2001)	Similar improvement in verum and placebo			
	Homeopathic immunotherapy (HIT) made with house dust potencies	1	Hardy (1984)	HIT better than placebo			
	Dust mite homeopathy vs placebo	1	Lewith et al 2002	No difference between active and placebo in FEV1, PEF, symptoms, use of b2-agonists, and asthma score			
	30c dilution grass pollen vs placebo	1	Reilly et al 1986	↓ Symptom score, visual analog scale, and use of antihistamines			
	30c dilution of various allergens vs placebo	1	Taylor et al 2000	↑ PNIF morning and evening; no difference between groups in visual analog scale and symptom score (N = 50)			
				There was a mean reduction of the visual analogue scale score of 10.9 mm in the homeopathy group compared with 1.1 mm in the placebo group (95% confidence interval for difference 4.2 to 15.4, P = 0.0007 after two weeks treatment (N = 253) (29)			
Nasal Luffa compositum Heel vs Nasal cromone	1	Weiser et al 1999	Homeopathy = nasal cromone, both effective on symptoms				
Individual homeopathy plus drugs vs placebo plus drugs	1	White et al 2003	No difference between active and placebo in asthma-related QOL, PEF, use of β2-agonists, missing days				
Homeopathic grass, trees, weeds mix vs placebo	1	Kim et al 2005	Significant improvement in active group in 3 QOL questionnaires; no mention of clinical symptoms				



	Galphimia homeopathic dilution vs Conventional dilution/placebo	3	Wiesenauer and Gaus 1985	No significant difference between active and placebo treatments			
	Galphimia 2c versus placebo		Wiesenauer and Ludtke (1987)	Significantly less eye symptoms in verum group			
	Galphimia 4D versus placebo		Wiesenauer and Ludtke (1995)	Significant relief in verum group			
	Galphimia homeopathic dilution vs placebo		Lüdtke 1997	The overall rate of improved eye-symptoms is about 1.25 (CI: 1.09 to 1.43) times higher in the verum than in the placebo group. Across the single studies (7 RCT's) the results were highly comparable except for the study run in 1985.		A significant superiority of Galphimia glauca over placebo is demonstrated. Estimates of verum success rates are comparable with those of conventional antihistaminics, but no side effects occurred. As not all of the single studies were analyzed by intention to treat analysis the results may be biased. (63)	
			Linde 1997	The pooled odds ratio for ocular symptoms at 4 weeks was 2.03 (1.51 to 2.74) with a similar result for nasal symptoms (30)			



18) *Adverse effects (42, 65, 66)*

Outcome	review	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Adverse effect	Dantas 2000	19 19 12	RCT case reports homeopathic pathogenetic trials	in therapeutic clinical trials the incidence of reported adverse effects (AEs) is higher in the verum group than in the placebo group (mean incidence 9.4/6.1).		Homeopathic medicines in high dilutions, prescribed by trained professionals, are probably safe and unlikely to provoke severe adverse reactions. It is difficult to draw definite conclusions due to the low methodological quality of reports claiming possible adverse effects of homeopathic medicines.	
Aggravations	Grabia 2003	24	RCT's	In total, 50 aggravations were attributed to patients treated with placebo and 63 to patients treated with homeopathically diluted remedies		the data from placebo- controlled, double-blind RCTs of homeopathy mentioning the phenomenon of homeopathic aggravations do not provide support for the existence of aggravations.	24 RCT's, not 25
Delayed diagnosis	Lim 2010			Mouth ulcers Seizure and apnoea Malnutrition, sepsis and death Malnutrition and oedema Homeopathy for epilepsy instead of anticonvulsants			

Dantas et al. 2000(65) are confirmed by Fisher 2002 (67). His conclusions are:

- Homeopathic medicines may provoke adverse events, but these are generally mild and transient
- There is under-reporting.
- There are cases of 'mistaken identity', where herbal and other medicines were described as homeopathic.
- The main risks associated with homeopathy are indirect, relating to the prescriber rather than the medicine.

Lim et al. (66) report on delayed hospitalization in Australian children due to

- malnutrition in infants using homeopathy and dietary restriction for chronic eczema
- homeopathy for epilepsy instead of anticonvulsants
- seizure and apnoea using homeopathic medicines

We have to be aware of this reality. In the hands of homeopaths without any medical training, asthma and convulsions might not be recognized as severe disease where seizure can be deathly or lead to severe damage of the brain. For chronic eczema, where patients are desperate, an overly restrictive diet can lead to malnutrition in infants, which again might not be recognized by non-medical homeopaths.



ADDITIONAL REVIEWS FOUND

We do not know why these reviews were not found or were excluded by the KCE (on exception of papers before 2000).

1) Upper respiratory tract infections (URTI)(18, 21)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Acute rhinitis	Eupatorium perfoliatum 2x versus aspirin	2	Gassinger et al. (1981)	Equivalence between homeopathy and allopathy		In summary, there is an efficacy/ effectiveness paradox (similar to that found in several other areas of complementary medicine research) with a weak evidence in favor of homeopathy when studies are done in randomized and double-blind conditions	
Acute rhinitis	Homeopathic complex Grippeheel versus aspirin		Maiwald et al. (1988)	Equivalence between homeopathy and allopathy			
Cough	Low-dilution (3c) homeopathic complex in syrup (Drosera) versus placebo	1	Bordes and Dorfman (1986)	Decrease of symptoms 20 out of 30 treated patients, as against only 8 out of 30 in the placebo group			
Sinusitis	Low-dilution (3x-4x) homeopathic complex Luffa, Cinnabaris, Kalium bichromicum versus placebo	1	Wiesenauer et al. (1989)	No effect over placebo			
Chronic sinusitis	Euphorbium compositum versus placebo	1	Weiser and Clasen (1994)	21.1% improvement in the verum group, 14.4% in the placebo group. No change in tests			
Common cold and flu	Engystol-N versus placebo, i.v. injection	1	Heilmann (1994)	No change of frequency of attacks, decrease of symptoms and their duration			
	Oscillococcinum		Ferley 1989	significance for homeopathy			
	Oscillococcinum		Papp 1998	significance for homeopathy			
Pharyngitis, tonsillitis	Individualized versus placebo	1	De Lange de Klerk (1999)*	Little, non significant, effect in favor of homeopathy versus placebo			
Acute otitis media	Individualized versus placebo	1	Jacobs (2001)*	Less failures in verum group, not significant; little and significant decrease of symptoms in verum group			
	homeopathic therapy vs. conventional therapy	1	Harrison 1999	equivalence/ trend for homeopathy			



Chemotherapy-associated stomatitis	Homeopathic complex Traumeel-S versus placebo.	1	Oberbaum et al. (2001)*	Less stomatitis in verum group			
Upper respiratory tract infections	Homeopathic complex L52 versus placebo	3	Lecoq (1985) (50)	Patients rated more relief in verum group			
	Individualized versus untreated		Steinsbekk et al. (2005)*	Decrease of days with symptoms in homeopathic group			
	Individualized, parents-selected, versus placebo		Steinsbekk et al. (2005)*	No effectiveness of homeopathy over placebo			
adenoid vegetations	sequence of four homeopathic medications	1	Friese 2001	no advantage, high placebo responder rate			

*children

Bellavite et al. 2006 (21) searched the literature between 1978 and 2006 and found 12 RCTs concerning upper respiratory tract conditions. Of these 12 RCT, eight of them report a positive improvement in favour of homeopathy. Three of them (De Lange de Klerk (1999)*, Jacobs (2001)*, Steinsbekk et al. (2005)*) are also reported by Altunc (15).

Börnhoft et al. 2006(18) added another four studies, yet not included by Bellavite 2006: Ferley 1989, Papp 1998, Harrison 1999 and Friese 2001. These studies add evidence for the efficacy of homeopathy in upper respiratory tract infections (eleven RCTs report a positive result out of 16 RCTs). Based on a meta-analysis of eight RCTs, Shang et al. 2005 (1) also found a positive effect for homeopathy in upper respiratory tract infections.



2) Allergic conditions(18, 28)

Outcome	Intervention/comp arison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Allergic asthma	Allopathy p allergen 30c (HIT) versus allopathy p placebo	4	Campbell et al. (1990); Reilly et al. (1994)	Less symptoms in verum group than placebo, no difference in tests		In summary, there is an efficacy/effectiveness paradox (similar to that found in several other areas of complementary medicine research) with a weak evidence in favor of homeopathy when studies are done in randomized and double-blind conditions	
	Homeopathic complex Engystol-N versus placebo		Matusiewicz 1995, 1996, 1997	Clinical improvement only in verum group			
	Individualized versus placebo		Lara-Marquez et al. (1997)	Verum better than placebo, significant changes of laboratory markers			
	Individualized versus placebo		Riveron-Garrote et al. (1998)	Higher reduction of asthma attacks in verum group			

These four additional RCTs, not mentioned by McCarney et al.(39), report a difference between the verum and placebo group for (allergic) asthma. Two studies used individualized homeopathy, the third used the homeopathic complex Engystol-N. The authors' conclusions include the RCTs mentioned by McCarney.

When taking into account the evidence from the table of upper respiratory tract infections (1), allergic rhinitis (17) and allergic conditions (2), Böhnhoft (18) conclude that there is a positive overall result in favour of homeopathy.

3) Vertigo (46)

Outcome	Intervention/comp arison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
vertigo	Vertigo-heel vs betahistine	2	Weiser 1998	Non-inferiority proved	In the meta-analyses are included 2 RCTs and 2 observational studies	Non-inferiority proved for vertigo-heel vs betahistine and Ginkgo-biloba for vertigo	
	Vertigo-heel vs Ginkgo-biloba		Issing 2004	Non-inferiority proved			

Schneider et al.(46) conclude that Vertigo-Heel is non-inferior in the treatment of vertigo in comparison with Betahistine or Ginkgo-Biloba.



4) Osteoarthritis(25-27)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Knee pain	Rhus toxicodendron 12x, Causticum 12x and Lac Vaccinum 12x vs 2 600 mg paracetamol/ day	3	Shiplely 1983	No difference between the two groups		Although promising, the evidence was inconclusive because of the paucity of evidence	
Hip or knee pain	Rhus toxicodendron 6x vs fenoprofen 600 mg 3 x / day		Shealy 1998	homeopathy significantly inferior to fenoprofen			
	Spiroflor (local application) vs piroxicam gel (0,5%)		Van Haselen 2000	No difference between the two groups			
Osteoarthritis	2 mL intra-articular injections per week of Zeel vs 2mL injection per week of Hyalart (a brand of hyaluronic acid)	1	Nahler 1998	No difference between the two groups		a positive trend towards the effectiveness of combination homeopathic preparations for the treatment of patients with OA. However, the small number of trials performed to date preclude firm conclusions as to the effectiveness of combination homeopathic remedies for this indication.	

De Silva et al. 2011(26) report on only three of the four trials Long et al. 2001(27) reported. Long et al. added one study with Zeel vs Hyalart. De Silva copied the conclusion of Long: although promising, the evidence was inconclusive because of the paucity of evidence. The major limitation in reviewing the evidence is the paucity of randomized controlled trials in the area: widening the evidence base, particularly for those compounds for which there is promising evidence, should be a priority for both researchers and funders. Weiner et al. 2004 (51) also report these four trials of Long. He concludes: collectively these data favour homeopathic treatment over placebo. However, the small number of studies prevents any firm conclusions about the efficacy of homeopathy for OA. He added the follow recommendation for use: even though the basic assumptions of homeopathy fly in the face of science, there is some trial evidence that homeopathic remedies might be superior to placebo in the treatment of rheumatic conditions, particularly RA and OA. However, there is no evidence to suggest that homeopathy is equivalent or superior to the efficacy of conventional therapy for persistent musculoskeletal pain since no studies were found investigating musculoskeletal pain.



5) Influenza like syndrome (47)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Treatment of influenza like syndrome	Oscillococcinum versus placebo	4	Ferley 1989 Papp 1998 Casanova 1992 (unpublished) Nolleaux 1990 (unpublished)	Oscillococcinum treatment reduced length of influenza illness by 0.28 days (95% confidence interval 0.50 to 0.06). Oscillococcinum also increased the chance of a patient considering treatment effective (relative risk 1.08; 95% CI 1.17, 1).		Though promising, the data were not strong enough to make a general recommendation to use Oscillococcinum for first-line treatment of influenza and influenza-like syndromes. Further research is warranted but the required sample sizes are large. Current evidence does not support a preventative effect of Oscillococcinum-like homeopathic medicines in influenza and influenza-like syndromes.	
Prevention of influenza like syndrome		3	Casanova 1984 Rottey 1995 Attina 1995	There was no evidence that homoeopathic treatment can prevent influenza-like syndrome (relative risk (RR) 0.64, 95% confidence interval (CI) 0.28 to 1.43)			

Vickers et al. 2006(47) conclude with: Though promising, the data were not strong enough to make a general recommendation to use Oscillococcinum for first-line treatment of influenza and influenza-like syndromes. Further research is warranted but the required sample sizes are large. Current evidence does not support a preventative effect of Oscillococcinum-like homeopathic medicines in influenza and influenza-like syndromes.



6) Prevention of migraine and headache (48, 68)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
migraine	Four single doses of 30C potencies of a choice of 6 remedies given orally in 2-week intervals	4	Brigo (1991)	Compared to placebo, significant improvement in all variables		There is insufficient evidence to support or refute the use of homeopathy for managing tension type, cervicogenic, or migraine headache.(48) In conclusion, this systematic review has not produced compelling evidence to suggest that individualized homeopathic treatment is more effective than placebo in the prevention of migraine or headache attacks. However, due to several caveats (e.g., paucity of RCTs) it seems premature to make final judgment on this matter.(68)	
	Choice of 60 remedies in D30, D200, and 1M potencies prescribed individually at monthly consultations with homeopathic		Straumsheim (1997)	No intergroup differences in terms of frequency, intensity, or duration of attacks nor analgesic consumption. Only sign (P = 0.05) of difference = neurologist's assessment of attack frequency			
	Choice of 11 remedies (all 30C) prescribed individually, 2 tablets twice weekly for 3 months		Whitmarsh (1997)	Homeopath = -19% placebo = -16% no sign of intergroup difference			
Chronic Headache	Free choice of individualized remedies for 12 weeks	Walach (1997)	Improvements in both groups, no intergroup difference				

Owen et al. 2004(48) includes the same four RCTs that Ernst et al.(68) included in 1999. Owen's conclusions are not very different from those of Ernst. There is insufficient evidence to support or refute the use of homeopathy for managing tension type cervicogenic or migraine headache. The studies reviewed possessed several flaws in design. Given these findings, further research is warranted to better investigate the effectiveness of homeopathic treatment of headaches.

Ernst et al.(68) concluded that the result of this systematic review suggests that homeopathic remedies are not superior to placebo in preventing migraine or headache.



Evidence for the efficacy of homeopathy from before 2000

1) Post-operative ileus(31)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
Post-operative ileus	Homeopathy (<i>Opium, Raphanus sativus, China regia, Arnica Montana</i>) versus placebo	1	Castelin 1997	Positive effect for homeopathy compared with placebo, on the time to first flatus		The WMD in the time to first flatus between homeopathy and placebo was shown to be -7.4 hours in favor of homeopathy (95% CI -4.0 to -10.8 hours). This effect is statistically significant ($p < 0.05$) and also likely to be clinically relevant. There is evidence that homeopathic treatment can reduce the duration of ileus after abdominal or gynecologic surgery. However, several caveats preclude a definitive judgment. These results should form the basis of a randomized controlled trial to resolve the issue.	
		1	Valero 1981	Positive effect for homeopathy compared with placebo, on the time to first flatus			
		1	Chevrel 1984	Positive effect for homeopathy compared with placebo, on the time to first flatus			
		1	Aulagnier 1985	Positive effect for homeopathy compared with placebo, on the time to first flatus			
		1	Grecho 1989	No difference			
		1	Dorfman 1992	Positive effect for homeopathy compared with placebo, on the time to first flatus			
		5	Linde 1997	pooled mean effect-size-difference of -0.22 standard deviations (95% CI -0.36, -0.09) for flatus, and -0.18 SDs (-0.33, -0.03) for stool (both $p < 0.05$)		Although the pooled effect-size-difference in this series was in favour of homeopathy, the largest and best performed trial had a negative outcome, which was the opposite of the effect reported in the other four trials.	

Barnes et al. 1997 (31) report that there is evidence that homeopathic treatment can reduce the duration of ileus after abdominal or gynaecological surgery. However, several caveats preclude a definitive judgment. These results should form the basis of a randomized controlled trial to resolve the issue. This evidence is confirmed by the meta-analysis performed by Linde et al. 1997(30) who conclude that, although the pooled effect-size-difference in this series was in favour of homeopathy, the largest and best performed trial had a negative outcome, which was the opposite of the effect reported in the other four trials.

Meta-analyses



Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
All	All/placebo, conventional	107	Kleijnen et al. 1991	81 trials reported positive results; most trials low-quality, but many exceptions		Available evidence positive but not sufficient to draw definitive conclusions	
	All/placebo	89	Linde et al. 1997	OR of all trials over placebo, 2.45 (95% CI, 2.05–2.93); in better trials, 1.66 (CI, 1.33–2.08)		Results not compatible with the hypothesis that all homeopathy is placebo; no firm evidence for any single condition	
	Classical/placebo, conventional	32	Linde and Melchart 1998	Responder RR vs. placebo, 1.62 (CI, 1.17–2.23); in better-quality trials, 1.12 (CI, 0.87–1.44)		Available evidence suggests effects over placebo; evidence not convincing because of shortcomings and inconsistencies	
	All/placebo	17	Cucherat et al. 2000	Combined <i>p</i> -value for an effect over placebo < 0.001; for best trials only, <i>p</i> < 0.08		Some evidence suggests homeopathy more than effective placebo; studies of high quality more likely to be negative	
	All (unknown)/placebo, conventional	8/110 vs 6 conventional	Shang et al. 2005	OR = 0.88 (CI 0.65– 1.19) for homeopathy vs. placebo (i.e. no difference); OR = 0.58 (CI 0.39–0.85) for conventional trials (i.e. significant difference)		Effects of homeopathy indistinguishable from placebo, while effects of conventional trials remain different from placebo	

Six meta-analyses have been done in homeopathy. Ernst et al. 1999(69) has been excluded for inclusion shortcomings. He reported on 3 RCTs and 3 CCTs (controlled clinical trials).

Five have been done before 2000, Shang(1) is published in 2005.

Four meta-analyses(20, 30, 70, 71) report an effect of homeopathy superior to placebo. Shang et al. 2005 has some important methodological shortcomings.



Health Technology Assessment (HTA) report (18)

Bornhoft G, Wolf U, von Ammon K, Righetti M, Maxion-Bergemann S, Baumgartner S, et al. Effectiveness, safety and cost-effectiveness of homeopathy in general practice - summarized health technology assessment. *Forsch Komplementmed.* 2006;13 Suppl 2:19-29.(18)

Outcome	Intervention/comparison	N RCT	Based on studies	Results	Comments	Authors conclusions	Assessment
All			22 reviews including 4 meta-analyses			taking internal and external validity criteria into account, effectiveness of homeopathy can be supported by clinical evidence	
Upper respiratory tract infections and allergic conditions			16 single RCT's			8 of 16 RCT's were significant in favor of homeopathy	

Bornhoft et al. 2006 (18) conclude that taking internal and external validity criteria into account, effectiveness of homeopathy can be supported by clinical evidence.



DISCUSSION AND FINDINGS:

To generate evidence at the highest level, several RCTs have to be done with the **same** homeopathic medicine for the same diagnosis.

This report summarizes the findings of 49 reviews on homeopathy on 20 different conditions. In total 119 RCTs have been included (see table 1) of which 12 RCTs are mentioned twice. References of the included RCTs can be found in the ANNEX document.

We identified 107 different RCTs that have been published all using **different approaches** in homeopathy and in **different conditions**. This is 0,05 % of all publications concerning RCTs. For acupuncture there are in the same period 1274 RCTs published (0,4% of all publications). So without doing any review, it is clear that extensive evidence in homeopathy at the highest level is not likely to be achieved.

There are a few exceptions: for example, fibromyalgia. All four trials on fibromyalgia report positive outcomes; although the sample size of each trial is small, they are well conducted. Two trials report on individualized homeopathy, the two others used specific homeopathic remedies. Such heterogeneity of study design makes meta-analysis problematic.

The Health Technology Assessment (HTA) report of the Swiss Federal Office for Public Health concluded: taking internal and external validity criteria into account, effectiveness of homeopathy can be supported by clinical evidence. Professional and adequate application can be regarded as safe (18).

Four (20, 30, 70, 71) out of five meta-analyses conclude that homeopathy is more than a placebo effect. Shang et al. (1) conclude that the clinical effects of homeopathy are placebo effects. On the other hand, they concluded that the overall quality of homeopathic trials was superior to those of conventional trials.

By excluding the reviews of Börnhoff et al. 2006(18) and Bellavite et al.(21, 28), the KCE report excluded the most common reasons patients consult a homeopathic practitioner, namely upper respiratory tract infections and allergic conditions (Witt et al. 2005 (51)).



There is evidence for the efficacy of homeopathic remedies in single conditions.

There is convincing evidence for the efficacy of Aconitum in post-operative agitation in children (13-15).

There is convincing evidence of efficacy of Belladonna 7cH and X-ray 15cH (Balzarini 2000) (16) and topical calendula (Pommier 2004) (17) for the treatment of radiodermatitis and for Traumeel S for the treatment of chemotherapy-induced stomatitis (Oberbaum 2001) (16-18).

There is evidence for the efficacy of homeopathy for diarrhoea in childhood. This is confirmed by two meta-analyses (18-20).

There is strong evidence that homeopathy works for upper respiratory tract infections (URTI) (1, 18, 21, 22).

Ullman et al. (23) reported that homeopathic medicine may play a useful role as an adjunctive and/or alternative therapy for HIV.

Oscillocochinum can treat influenza-like symptoms (24).

Some evidence exists to support the superiority of homeopathic remedies over placebo for treating osteoarthritis and rheumatoid arthritis (25-27).

The evidence for the efficacy of homeopathy in fibromyalgia is based on four RCTs which all reporting positive results. (10)

When taking into account the evidence for upper respiratory tract infections, allergic rhinitis and allergic conditions, we conclude that there is a positive overall result in favour of homeopathy for these three conditions. (18, 21, 28)

Evidence of homeopathic efficacy from before 2000 in single conditions:

Isopathic nosodes were different from placebo on both subjective and objective measures for allergic conditions (29).

The available evidence is positive for post-operative ileus (1, 30, 31).

Galphimia glauca is statistically significantly more effective than placebo for seasonal allergy (30, 32).



Conclusion:

It is clear that the search to highest clinical level of evidence for homeopathy reported by the KCE report is of poor quality, conclusions are clearly questionable:

- 1) reviews are included who didn't include any clinical trial on homeopathy (4-6)
- 2) references are wrongly used and doesn't concern the trials included (6, 38)
- 3) the content of the reviews is poorly reported and contains a number of errors (4, 6, 12, 14, 15, 39-42)
- 4) references are not correctly cited (15, 33-35, 41, 43, 44)
- 5) authors conclusions not correctly reported (35)
- 6) reviews not included by KCE (10, 11, 18, 21, 23, 26, 28, 45-49). We don't know if this reviews were not found or excluded for some reason.
- 7) the exclusion of reviews with search date before 2000 has led to a misrepresentation of the evidence overall



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Table 1

Condition	N RCTs
insomnia	5
low back pain	1
induction of labour	2
chronic fatigue syndrome	2
dementia	0
wandering in dementia	0
chronic asthma	6
eneuresis	0
depression	2
anxiety	8
cancer related symptoms	8
childhood ailments	17
fibromyalgia	4
HIV	3
chronic venous insufficiency	1
premenstrual syndrome	2
allergic rhinitis	13
URTI	16
allergic conditions	7
vertigo	2
osteo-arthritis	3
influenza like syndrome	7
prevention of migraine and headache	4
post-operative ileus	6
TOTAL	119