Effectiveness of Homeopathy for Clinical Conditions:

Evaluation of the Evidence

Review of Submitted Literature

Prepared for the NHMRC Homeopathy Working Committee
by Optum

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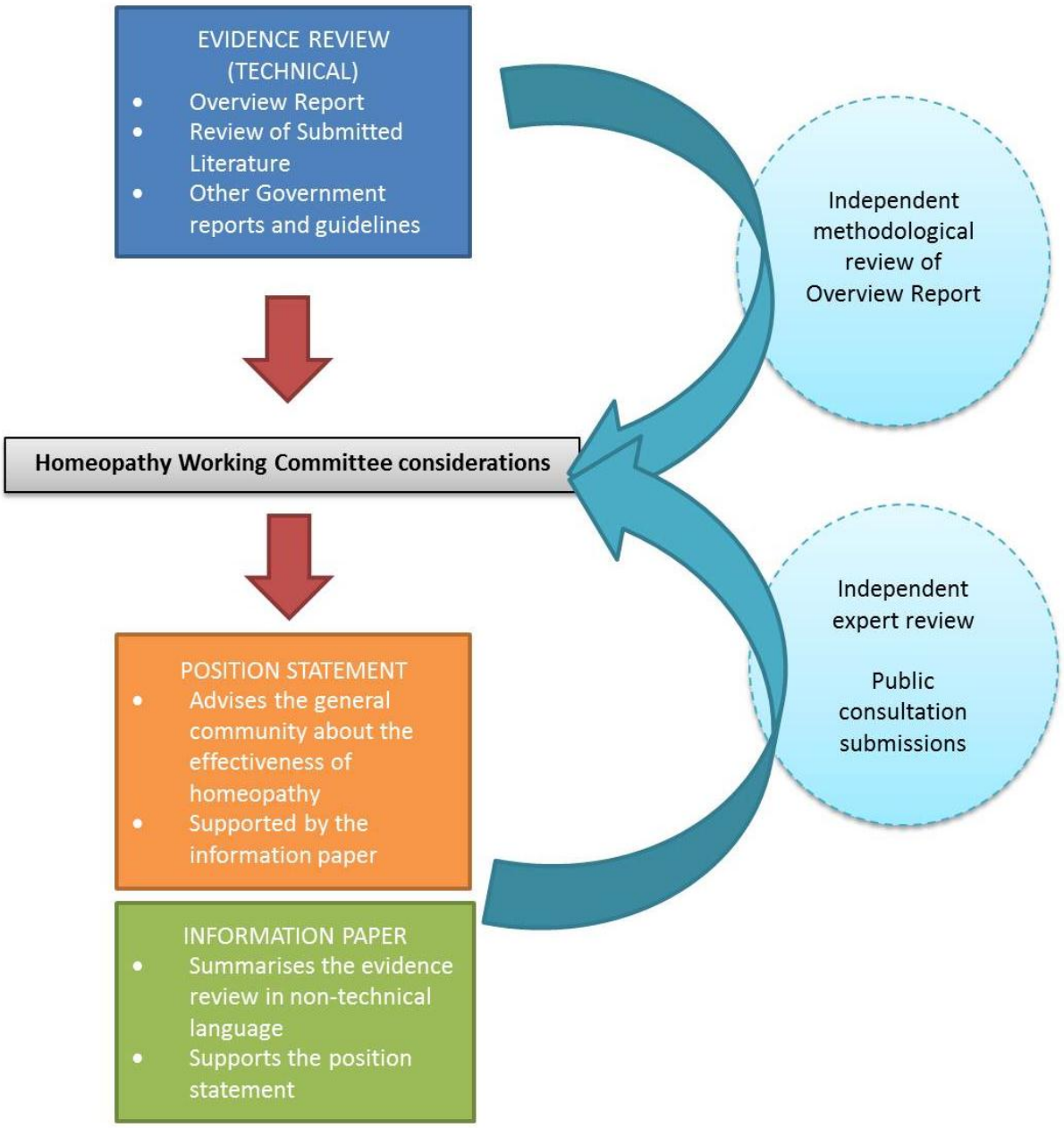
List of Abbreviations

DOMS	Delayed onset muscle soreness
HWC	Homeopathy Working Committee
MADRS	Montgomery and Asberg Depression Rating Scale
NHMRC	National Health and Medical Research Council
SIGN	Scottish Intercollegiate Guidelines Network
VAS	Visual Analogue Scale

1 Introduction

The purpose of this Review of Submitted Literature is to review and evaluate the individual studies submitted to the National Health and Medical Research Council (NHMRC) as potential evidence of the clinical effectiveness of homeopathy for any clinical condition. The literature was submitted by the Australian Homoeopathy Association, the Australian Medical Fellowship of Homeopathy and members of the public. This report accompanies the Overview Report on the effectiveness of homeopathy for any clinical condition. Both reports have been prepared by Health Technology Analysts Pty Ltd (the evidence reviewer, trading as Optum), in conjunction with the Homeopathy Working Committee (HWC). They will be considered in the development of an Information Paper to summarise the evidence on the effectiveness of homeopathy for the treatment of clinical conditions. They will also be considered in the development of a Position Statement to declare NHMRC's position on homeopathy as a treatment for clinical conditions, including the rationale for that position (**Figure 1)**.

Figure 1. Effectiveness of homeopathy for clinical conditions: project flow chart



2 Review of submitted literature

2.1 Methodology

2.1.1 Study eligibility

All of the submitted literature was assessed and categorised as either 'in scope' or 'out of scope'. 'In scope' literature included articles that had addressed the primary clinical research question:

- For patients with a specific clinical condition, is homeopathy an effective treatment, compared with no homeopathy/other treatments?

For the purpose of this evaluation, literature addressing the following topics was considered 'out of scope' and was not considered any further in the evaluation:

- Homeopathy for preventative/prophylactic use
- Homeopathy used in conjunction with other therapies, where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)

All 'in scope' literature was graded according to NHMRC's levels of evidence (NHMRC, 2009). The following *a priori* exclusion criteria were applied to the 'in scope' literature:

- Systematic review already included in the Overview Report
- Systematic review had been considered, but subsequently excluded from the Overview Report for reasons such as wrong intervention, wrong outcomes, study not published in the English language and superseded systematic review by the same authors
- Study already included within a systematic review in the Overview Report
- *Wrong research type or publication type.* Studies that were not systematic reviews, meta-analyses or prospectively designed and controlled studies (including randomised controlled trials, pseudo-randomised controlled trials, non-randomised controlled trials and prospective cohort studies) were excluded. Editorials, comments, book chapters, animal studies, correspondence, and news items were excluded. Studies were also excluded if they were not reported in full (e.g. research or systematic review protocols, conference proceedings, articles published in abstract form)
- *Wrong intervention*. Study did not investigate the effect of homeopathy
- *Wrong outcomes*. Study did not include outcomes relevant to the primary research question
- Study not published in the English language

The excluded articles are documented, with their level of evidence (where it could be assigned) and reasons for exclusion in **Appendix A.**

2.1.2 Critical appraisal and data extraction

Full citation details for the final list of included studies are provided in **Appendix B**. Each included study from the submitted literature was graded according to NHMRC's levels of evidence (NHMRC, 2009) and then quality appraised and the data extracted. Quality appraisal of the included studies

was carried out using the methodology checklists developed by the Scottish Intercollegiate Guidelines Network (SIGN) (SIGN, 2011). The methodological quality ratings of the study are based on an assessment of study design and risk of bias and are coded '++' if all or most of the criteria have been fulfilled. Where they have not been fulfilled, the conclusions of the study or review are thought very unlikely to alter. Studies rated '+' had some of the criteria fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions. Studies rated '-' had few or no criteria fulfilled. The conclusions of the study are thought likely or very likely to alter. The methodological quality rating code was then paired with an evidence level rating to provide an overall quality score. This was classified using the established hierarchical system as shown in **Table 1**. The quality assessment forms for the included studies are presented in **Appendix C**.

Table 1 SIGN levels of evidence for intervention studies (SIGN, 2011)

Score	Description
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs) or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies; high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2-	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (for example case reports, case series)
4	Expert opinion, formal consensus

Abbreviations: SIGN, Scottish Intercollegiate Guidelines Network.

Standardised NHMRC data extraction forms and evidence summary tables were used to capture information relevant to the review of the effectiveness of homeopathy in accordance with NHMRC standards. Extracted information included:

- General study details (citation, study design, evidence level, country and setting)
- Affiliations/sources of funds and conflicts of interest for each of the included studies
- Internal and external validity considerations
- Participant details, including key demographic characteristics
- Primary, secondary and other study outcome results

The data were extracted by one evidence reviewer. Data extraction forms for all of the included studies are presented in **Appendix C**.

2.2 Results of the review of submitted literature

2.2.1 Overview of the submitted literature

A total of 343 articles were submitted to the NHMRC. A review of their titles and abstracts found that a large majority of the articles (234 articles) were of the wrong research or publication type. A further 79 articles had already been included or considered in the Overview Report. Five articles

were excluded as they covered the wrong intervention (one article), outcomes (one article) or were not published in the English language (three articles). This resulted in 25 potentially relevant studies that were not included in the Overview Report and had assessed the effectiveness of homeopathy for the treatment of patients with a specific clinical condition, compared with no homeopathy/other treatments. Upon full text review of these 25 studies, nine were excluded as they examined homeopathy used in conjunction with other therapies, where the design of the study confounds the results and the specific effect of homeopathy cannot be determined. Three studies were excluded as they were the wrong research type or publication type, two studies were excluded as they did not report on efficacy outcomes and two studies were excluded as they were not published in English. This resulted in a final total of nine included studies – eight Level II studies and one Level III-2 study (**Table 2**).

Table 2 Summary of the application of the exclusion criteria to the submitted literature

Review of submitted literature	Total number of articles
Total number of submitted articles	**343**
Citations excluded after title/abstract review[a]	
Systematic review already included in the Overview Report	24
Systematic review had been considered but excluded from the Overview Report	11
Study already included within a systematic review in the Overview Report	44
Wrong research type or publication type	234
Wrong intervention	1
Wrong outcomes	1
Not in English	3
Number of articles reviewed in full text	**25**
Articles excluded after full text review[a]	
Homeopathy used in conjunction with other therapies, where the design of the study confounds the results and the specific effect of homeopathy cannot be determined	9
Wrong research type or publication type	3
Wrong outcomes	2
Not in English	2
Final number of included studies	**9**

[a] Excluded articles are documented, with their reasons for exclusion, in **Appendix A**.

The nine included studies assessed the effectiveness of homeopathy for the treatment of patients with a total of eight different clinical conditions, compared with no homeopathy/other treatments. Five of the eight conditions (otitis media, delayed-onset muscle soreness, depression, bruising, and sleep or circadian rhythm disturbances) were examined in the Overview Report. The remaining three clinical conditions (pain and postoperative recovery after total abdominal hysterectomy, tracheal secretions and wound healing after foot surgery) were not evaluated in the Overview Report as there were no relevant systematic reviews. The studies associated with these conditions have been critically appraised in the current report, but their findings will not be considered further as they are a self-selected sample and other literature concerning the effectiveness of homeopathy for those conditions has not been systematically retrieved.

All of the included studies contained limitations that should be considered in the evaluation of the evidence. In general, the evidence base for homeopathy is not of high quality and many of the individual studies were poorly designed, conducted and reported. In addition, most of the studies were small in size, had a high loss to follow up and were insufficiently powered to detect a statistically significant outcome. There was generally a lack of clarity around whether or not active comparators were appropriate. Furthermore, many primary studies investigated individualised homeopathy as the intervention. Whilst individualisation of therapy allows homeopathy to be practiced in its traditional fashion, this increases the complexity of comparing outcomes and determining the efficacy of specific homeopathic regimens.

2.2.2 Otitis media

One Level II study (Sinha et al, 2012; SIGN Evidence Level 1+) was identified that examined the effectiveness of individualised homeopathy for the treatment of children with acute otitis media, compared with conventional therapy (**Table 3**). Conventional therapy consisted of an 'observation option' for the first 3 days, where management was confined to symptomatic relief using analgesic, anti-inflammatory and antipyretics. In both homeopathy and conventional therapy groups, if less than 50% improvement was observed in the first 3 days of treatment, antibiotics were given.

However, the authors noted that no antibiotics were required for any case in the homeopathy group. Sinha et al (2012) was not included in any of the three relevant systematic reviews in the Overview Report as the study was published after the time of the systematic reviews. The results of this double-blind, Level II study of 81 participants reported a significant difference in favour of homeopathy on the number of children who were cured on the third day of treatment (p=0.000). There was no significant difference between homeopathy and conventional therapy in the number of children who were cured on the 7th, 10th or 21st day of treatment. There was also no significant difference in overall symptomatic improvement between the two groups. Sinha et al (2012) concluded that "individualised homeopathy is an effective conventional outcome in acute otitis media. There were no significant differences between groups in the main outcome. Symptomatic improvement was quicker in the homeopathy group and there was a large difference in antibiotic requirements favouring homeopathy".

The evidence reviewer notes that the Level II study by Sinha et al (2012) had an appropriate method of randomisation of subjects to treatment groups. The analysis was conducted by intention-to-treat analysis and loss to follow up was reported. However, the sample size was small (N=81 participants) and a method of allocation concealment was not described, which may have been a source of selection bias. There was also a risk of bias in measuring the severity of disease, as the parents/guardians were asked to subjectively rate the severity of symptoms of their child. Importantly, the only significant outcome detected in this study was a significant difference in favour of homeopathy for the number of children who were cured on the third day of treatment. However, the practical importance of this effect is questionable, given that the statistic was calculated from only 4/40 patients who were cured in the homeopathy group compared with 1/40 in the comparator group.

The addition of Sinha et al (2012) to the body of evidence for otitis media is consistent with the conclusion from the Overview Report that there is no reliable evidence that homeopathy is as effective as other therapies for the treatment of children with acute otitis media. However, this is a self-selected study and other literature concerning the effectiveness of homeopathy for otitis media has not been systematically retrieved.

Table 3 Evidence summary table of Sinha et al (2012) on the effectiveness of homeopathy for the treatment of acute otitis media

Study ID Level of evidence[a] *Quality*[b]	Patient population	Intervention	Comparator	Outcome	Results
Sinha et al (2012) [Level II] *SIGN EL 1+* N=81	Children with earache of not more than 36 hours duration. • Mean age 4±2 years • 50% male and 50% females	Individualised homeopathy in 50 LM potencies	Conventional therapy. An 'observation option' was adopted for the first 3 days: patients were given symptomatic treatment without antibiotics (may include analgesics, anti-pyretic, anti-inflammatories). If less than 50% improvement was observed in the first 3 days of treatment, antibiotics were given.	Cured on the 3rd day	Significant difference in favour of homeopathy (p=0.000) • Homeopathy group: 4/40 (10%) • Comparator group: 1/40 (2.5%)
				Cured on the 7th, 10th or 21st day	No significant difference
				Symptomatic improvement	No significant difference

Abbreviations: EL, Evidence level; LM, Millesimal scale; SIGN, Scottish Intercollegiate Guidelines Network.
[a] Level of evidence as assessed by the evidence reviewer.
[b] Study quality as assessed by the evidence reviewer using the methodology checklists developed by SIGN. An evidence level of '1' represents systematic reviews of RCTs or individual RCTs. An evidence level of '2' represents systematic reviews of case-control or cohort studies, or individual case-control or cohort studies. Quality ratings are based on an assessment of study design and risk of bias and are coded as '++', '+' or '-'. Studies of good quality are rated as '++', whilst poor quality studies are rated '-'.

2.2.3 Delayed-onset muscle soreness

Two Level II studies (Tveiten et al, 1998; Vickers et al, 1998) were identified that examined the effectiveness of homeopathy for the treatment of patients with delayed-onset muscle soreness (DOMS), compared with placebo (

Table 4). These studies were not included in either of the two relevant systematic reviews in the Overview Report as both studies were published after the time of the systematic reviews.

Tveiten et al (1998) (SIGN Evidence Level 1+) was a double-blind, placebo-controlled Level II study of 71 participants that investigated the effect of homeopathic *Arnica* D30 on cell damage and muscle soreness after long-distance running in a marathon. The results found that muscle soreness immediately after the marathon was significantly lower in the *Arnica* group compared with placebo as measured by the Visual Analogue Scale (VAS) (p=0.017). However, there was no difference between the homeopathy and placebo groups in the mean estimated muscle soreness for the entire treatment period of 3 days after the marathon as measured by VAS. There was also no significant difference between the two groups for cell damage as measured by enzymes, or in electrolytes and creatinine. No side effects were reported by either group. The authors concluded that "*Arnica* D30 had a positive effect on muscle soreness after marathon running, but not on cell damage as measured by enzymes".

The evidence reviewer notes that the Level II study by Tveiten et al (1998) had an appropriate method of allocation concealment and randomisation of subjects to treatment groups. However, the starting sample size was small (N=71), and a high percentage of participants (35% of total

participants; 27% (9/33) in the homeopathy and 33% (11/33) in the placebo groups) were lost to follow up which may have introduced selection bias. Additionally, a potential confounding factor that was not addressed by the authors is if the participants were permitted to consume other substances (e.g. sports drinks) after the marathon that may have had an effect on their recovery and the results of the trial. The authors' conclusion of the positive effect of *Arnica* D30 on muscle soreness after marathon running may be misleading, as there was no significant difference in muscle soreness between the homeopathy and placebo groups at any of the measured time points in the 3 days of treatment after the marathon.

Vickers et al (1998) (SIGN Evidence Level 1++) was also a double-blind, placebo-controlled Level II study of 400 participants that investigated the effect of homeopathic *Arnica Montana* 30X on muscles soreness after long-distance running races. The study was larger in size than Tveiten et al (1998), and the results found no significant difference between homeopathy and placebo in any of the mean 2-day VAS for soreness, Likert score for soreness or race time. Consequently, the authors concluded that "Homeopathic *Arnica* 30X is ineffective for muscle soreness following long-distance running" and "*Arnica* 30X does not reduce DOMS resulting from long-distance running. Homeopaths should not prescribe *Arnica* for this indication, and runners should be advised not to take it".

Overall, the Level II study by Vickers et al (1998) was adequately powered and of good methodological quality with appropriate randomisation and allocation concealment, low loss to follow up and intention to treat analysis. Similar to Tveiten et al (1998), however, a potential confounding factor that was not addressed by the authors is if the participants were permitted to consume other substances (e.g. sports drinks) after the running race that may have had an effect on their recovery and the results of the trial.

The addition of Tveiten et al (1998) and Vickers et al (1998) to the body of evidence for DOMS is consistent with the conclusion from the Overview Report that homeopathy is not more effective than placebo for the treatment of people with DOMS. However, these are self-selected studies and other literature concerning the effectiveness of homeopathy for DOMS has not been systematically retrieved.

Table 4 Evidence summary table of Tveiten et al (1998) and Vickers et al (1998) on the effectiveness of homeopathy for the treatment of delayed-onset muscle soreness

Study ID Level of evidence[a] *Quality*[b]	Patient population	Intervention	Comparator	Outcome	Results
Tveiten et al (1998) [Level II] *SIGN EL 1+* N=71	Participants entering the 1995 Oslo marathon	Arnica D30, 5 pills in the evening before the marathon and continued the morning and evening on the day of the run and for the following 3 days	Placebo	Muscle soreness immediately after the marathon as measured by VAS	Significantly lower in the Arnica group compared with placebo (p=0.017)
				Mean estimated muscle soreness for the entire treatment period as measured by VAS	No significant difference
				Cell damage measured by enzymes	No difference between the two groups
				Electrolytes and creatinine	No difference between the two groups
				Side effects	No side effects were reported in either group
Vickers et al (1998) [Level II] *SIGN EL 1+* N=400	Patients aged 18 years and over who must have experienced DOMS after long-distance running races	Arnica Montana 30X, 5 pills twice daily starting the evening before the race and continuing until 9 doses had been taken	Placebo	Mean 2-day VAS for soreness	No significant difference
				Likert score for soreness	No significant difference
				Race time	No significant difference

Abbreviations: D, Decimal scale; DOMS, Delayed onset muscle soreness; EL, Evidence level; SIGN, Scottish Intercollegiate Guidelines Network; VAS, Visual analogue scale.

[a] Level of evidence as assessed by the evidence reviewer.

[b] Study quality as assessed by the evidence reviewer using the methodology checklists developed by SIGN. An evidence level of '1' represents systematic reviews of RCTs or individual RCTs. An evidence level of '2' represents systematic reviews of case-control or cohort studies, or individual case-control or cohort studies. Quality ratings are based on an assessment of study design and risk of bias and are coded as '++', '+' or '-'. Studies of good quality are rated as '++', whilst poor quality studies are rated '-'.

2.2.4 Depression

One Level II study (Adler et al, 2009; SIGN Evidence Level 1+) was identified that investigated the non-inferiority and tolerability of individualised homeopathic medicines in acute depression using fluoxetine as an active control (**Table 5**). This study was not included in the one relevant systematic review in the Overview Report as it was published after the time of the systematic review. Adler et al (2009) was a double-blind, double-dummy Level II study of 91 participants where matching placebos for each active treatment were applied. Therefore, both the homeopathy and active comparator groups also received placebo tablets that appeared identical to their corresponding verum formulations. The study found no significant difference between homeopathy and fluoxetine in Montgomery and Asberg Depression Rating Scale (MADRS) scores, response rate, remission rate or tolerability. The authors concluded that "this study indicates the non-inferiority of individualised homeopathic Q-potencies as compared to fluoxetine in acute treatment of outpatients with moderate to severe depression".

The evidence reviewer notes that the Level II study by Adler et al (2009) utilised an appropriate method of randomisation and allocation concealment. However, the validity of the authors' conclusion is questionable as the sample size of the trial was small (N=91) and a high percentage of participants (40% of total participants; 40% (19/48) in the homeopathy and 40% (17/43) in the comparator groups) were lost to follow up. It is also unlikely that the study was sufficiently powered to detect non-inferiority. Furthermore, the authors did not address the potential confounding influence of concomitant psychoactive medications that were taken by some patients in both treatment groups.

The addition of Adler et al (2009) to the body of evidence for depression is consistent with the conclusion from the Overview Report that there is no reliable evidence that homeopathy is as effective as fluoxetine for the treatment of people with depression. However, this is a self-selected study and other literature concerning the effectiveness of homeopathy for depression has not been systematically retrieved.

Table 5 Evidence summary table of Adler et al (2009) on the effectiveness of homeopathy for the treatment of depression

Study ID Level of evidence[a] *Quality*[b]	Patient population	Intervention	Comparator	Outcome	Results
Adler et al (2009) [Level II] *SIGN EL 1++* N=91	Patients with moderate to severe depression	Individualised homeopathy. Various Q-potencies, one drop, 3 times a week in the morning; and matching placebo. Concomitant psychoactive medications: 1 patient using clonazepam, 1 patient using diazepam	20 mg fluoxetine-hydrochloride, once daily; and matching placebo Concomitant psychoactive medications: 3 patients taking clonazepam, 2 patients taking diazepam	MADRS scores	No significant difference. Individualised homeopathic Q-potencies were not inferior to fluoxetine
				Response rate	No significant difference
				Remission rate	No significant difference
				Tolerability (side effects rate)	No significant difference

Abbreviations: EL, Evidence level; MADRS, Montgomery and Asberg Depression Rating Scale; Q-potencies, Quinquagintamillesmial; SIGN, Scottish Intercollegiate Guidelines Network.
[a] Level of evidence as assessed by the evidence reviewer.
[b] Study quality as assessed by the evidence reviewer using the methodology checklists developed by SIGN. An evidence level of '1' represents systematic reviews of RCTs or individual RCTs. An evidence level of '2' represents systematic reviews of case-control or cohort studies, or individual case-control or cohort studies. Quality ratings are based on an assessment of study design and risk of bias and are coded as '++', '+' or '-'. Studies of good quality are rated as '++', whilst poor quality studies are rated '-'.

2.2.5 Bruising

One Level II study (Seeley et al, 2006; SIGN Evidence Level 1-) was identified that evaluated the efficacy of homeopathic *Arnica Montana* as an antiecchymotic agent when taken perioperatively by patients undergoing elective rhytidectomy, compared with placebo (**Table 6**). Seeley et al (2006) was not included in the one relevant systematic review in the Overview Report as the study was published after the time of the systematic review. Seeley et al (2006) was a double-blind, placebo-controlled Level II study of 29 participants that found no significant difference between homeopathy and placebo in a subjective assessment of bruising by the patient or nurse/physician using VAS. In an objective assessment using a newly designed computer model, there was also no significant difference between groups on the degree of colour change attributable to surgery. However, patients receiving homeopathic *Arnica Montana* were found to have a smaller area of ecchymosis on postoperative days 1, 5, 7 and 10 (i.e. all of the days of assessment using the computer model). These differences were statistically significant only on postoperative days 1 ($p<0.005$) and 7 ($p<0.001$). Overall, the authors concluded that "the computer model provides an efficient, objective and reproducible means with which to assess perioperative colour changes, both in terms of area and degree. Patients taking perioperative homeopathic *Arnica Montana* exhibited less ecchymosis, and that difference was statistically significant on two of the four postoperative data points evaluated".

The evidence reviewer notes that the Level II study by Seeley et al (2006) had an appropriate method of allocation concealment and randomisation of subjects to treatment groups. However, a number of biases were present in the study which may have affected the results. The starting sample size was small (N=29) and 20% of participants in the placebo group (3/15 participants) did not complete the VAS for subjective evaluation. Baseline demographics were not provided by the authors, so it is

unclear if the study groups were comparable at baseline. Additionally, this study used a newly designed computer model to assess perioperative colour changes, both in terms of area and degree. This model has not been validated and confirmed as an appropriate means to make these assessments, yet the only statistically significant results from this trial were measured from this model. Indeed, the validity of the results from the computer model is questionable, given that subjective assessment of bruising by VAS found no significant difference between homeopathy and placebo.

The addition of Seeley et al (2006) to the body of evidence for bruising is consistent with the conclusion from the Overview Report that there is no reliable evidence that homeopathy is more effective than placebo for the treatment of people with bruising. However, this is a self-selected study and other literature concerning the effectiveness of homeopathy for bruising has not been systematically retrieved.

Table 6 Evidence summary table of Seeley et al (2006) on the effectiveness of homeopathy for the treatment of bruising

Study ID Level of evidence[a] *Quality*[b]	Patient population	Intervention	Comparator	Outcome	Results
Seeley et al (2006) [Level II] *SIGN EL 1-* N=29	Patients undergoing elective rhytidectomy	SINECCH (Arnica Montana), once every 8 hours for 4 days postoperatively	Placebo	Subjective assessment by the patient using VAS	No significant difference
				Subjective assessment by the nurse/physician using VAS	No significant difference
				Degree of colour change attributable to surgery as measured by the computer model	No significant difference
				Reduction in ecchymosis as measured by the computer model	Significant difference in favour of homeopathy only on postoperative days 1 ($p<0.005$) and 7 ($p<0.001$). No significant difference on postoperative days 5 and 10

Abbreviations: EL, Evidence level; SIGN, Scottish Intercollegiate Guidelines Network; VAS, Visual Analogue Scale.
[a] Level of evidence as assessed by the evidence reviewer.
[b] Study quality as assessed by the evidence reviewer using the methodology checklists developed by SIGN. An evidence level of '1' represents systematic reviews of RCTs or individual RCTs. An evidence level of '2' represents systematic reviews of case-control or cohort studies, or individual case-control or cohort studies. Quality ratings are based on an assessment of study design and risk of bias and are coded as '++', '+' or '-'. Studies of good quality are rated as '++', whilst poor quality studies are rated '-'.

2.2.6 Sleep or circadian rhythm disturbances

One Level III-2 study (Waldschutz and Klein, 2008; SIGN Evidence Level 2-) was identified that assessed the non-inferiority of therapy with homeopathic Neurexan compared with Valerian therapy in patients with mild to moderate sleep onset and/or sleep maintenance insomnias (**Table 7**). This

study was not included in any of the four relevant systematic reviews in the Overview Report as these particular systematic reviews included only Level II studies.

Waldschutz and Klein (2008) was an open-label, prospective cohort study of 409 participants that was conducted in 89 German centres offering both conventional and complementary therapies. The study reported no significant difference between homeopathy and Valerian for all but two of the outcomes examined. After 14 days of treatment, duration of sleep had significantly increased in the homeopathy group compared with Valerian at days 8, 12 and 14 (p-value not reported). There were also significant improvements in daytime fatigue in favour of homeopathy ($p<0.05$). However, Neurexan was non-inferior to Valerian on all variables assessed. Overall, the authors concluded that "for patients favourable towards a complementary and alternative medicine-based therapy, Neurexan might be an effective and well-tolerated alternative to conventional Valerian-based therapies for the treatment of mild to moderate insomnia. The results suggest greater short-term effects with Neurexan on sleep duration and on daytime fatigue after 1 month of treatment".

The evidence reviewer notes that the authors' conclusion is subject to a high risk of bias due to the non-randomised, open-label, cohort design, which is not the best study type to investigate non-inferiority and the effectiveness of Neurexan on patients with mild to moderate sleep onset and/or maintenance insomnias. In addition, the efficacy of the comparator (Valerian) is not well established in the literature for this indication. A high percentage of participants were lost to follow up (22% of total participants; 21% (41/197) in the homeopathy and 23% (48/212) in the comparator groups) and the results may also have been affected by the variable dosage of Valerian in the comparator group, which was subject to the physician's judgement. The practical importance of the significant effect of Neurexan on sleep duration at days 8, 12 and 14 is questionable, as this outcome was measured daily and there was no difference in sleep duration between treatment groups for the other 11 days that the outcome was measured.

The addition of Waldschutz and Klein (2008) introduces a lower level of evidence study to the body of evidence for sleep or circadian rhythm disturbances in the Overview Report. Nevertheless, the results of Waldschutz and Klein (2008) are consistent with the conclusion from the Overview Report that there is no reliable evidence that homeopathy is more effective than placebo for the treatment of people with sleep or circadian rhythm disturbances. However, this is a self-selected study and other literature concerning the effectiveness of homeopathy for sleep or circadian rhythm disturbances has not been systematically retrieved.

Table 7 Evidence summary table of Waldschutz and Klein (2008) on the effectiveness of homeopathy for the treatment of sleep disorders

Study ID Level of evidence[a] *Quality*[b]	Patient population	Intervention	Comparator	Outcome	Results
Waldschutz and Klein (2008) [Level III-2] *SIGN EL 2-* N=409	Patients with mild to moderate sleep onset and/or sleep maintenance insomnias	Homeopathic Neurexanfor 28 days. Dosage at physician's judgements	Valerian. Dosage at physician's judgement	Improvements in sleep latency after 14 days' treatment	No significant difference
				Duration of sleep after 14 days' treatment (measured daily)	Significantly favoured Neurexan therapy at days 8, 12 and 14 (p-value not reported) • Homeopathy group: duration increased by 2.2±1.6 hours • Comparator group: duration increased by 2.0±1.5 hours
				Sleep quality at day 28	No significant difference
				Daytime fatigue	Significant improvement in favour of Neurexan (p<0.05) • Homeopathy group: 49% reported no daytime fatigue • Comparator group: 32% reported no daytime fatigue
				Time of first signs of improvement	No significant difference
				Overall effectiveness	No significant difference
				Overall symptomatic change since beginning of therapy	No significant difference
				Adverse event	1 case of mild caffeine intolerance associated with Neurexan after 9 days of treatment
				Mean blood pressure	No significant difference
				Compliance rate	No significant difference

Abbreviations: EL, Evidence level; SIGN, Scottish Intercollegiate Guidelines Network.
[a] Level of evidence as assessed by the evidence reviewer.
[b] Study quality as assessed by the evidence reviewer using the methodology checklists developed by SIGN. An evidence level of '1' represents systematic reviews of RCTs or individual RCTs. An evidence level of '2' represents systematic reviews of case-control or cohort studies, or individual case-control or cohort studies. Quality ratings are based on an assessment of study design and risk of bias and are coded as '++', '+' or '-'. Studies of good quality are rated as '++', whilst poor quality studies are rated '-'.

2.2.7 Pain and postoperative recovery after total abdominal hysterectomy

One Level II study (Hart et al, 1997; SIGN Evidence Level 1-) was identified that assessed the effects of homeopathic *Arnica* C30 on pain and postoperative recovery after total abdominal hysterectomy in women, compared with placebo (**Table 8**). This clinical condition was not included in the Overview Report as there were no relevant systematic reviews. Hart et al (1997) was a double-blind, placebo-

controlled Level II study of 93 participants that found no significant difference between the homeopathy and placebo groups for any of the outcomes examined, including infection rate following surgery, median time spent in hospital, pain at 2-week follow up, analgesic intake or mean pain score over 5 days as measured by VAS. The authors concluded that "*Arnica* in homeopathic potency had no effect on postoperative recovery in the context of our study".

The evidence reviewer notes that the Level II study by Hart et al (1997) had an appropriate method of randomisation of subjects to treatment groups. However, the study was subject to a high risk of bias. Selection bias may be present as a method of allocation concealment was not reported. The sample size was small (N=93) and a high percentage of participants were lost to follow up (22% of total participants; 19% (9/47) from the homeopathy and 24% (11/46) from the placebo groups). Importantly, all patients were permitted to remain on analgesics, non-steroidal anti-inflammatories and opioids during the course of treatment, which are likely to have confounded the results of the study. The findings by Hart et al (1997) cannot be interpreted further as the study is a self-selected sample and other literature concerning the effectiveness of homeopathy for pain and postoperative recovery after total abdominal hysterectomy has not been systematically retrieved.

Table 8 Evidence summary table of Hart et al (1997) on the effectiveness of homeopathy for the treatment of pain and postoperative recovery after total abdominal hysterectomy

Study ID Level of evidence[a] *Quality*[b]	Patient population	Intervention	Comparator	Outcome	Results
Hart et al (1997) [Level II] *SIGN EL 1-* N=93	Women booked for total abdominal hysterectomies at the Princess Anne Hospital, Southampton	Two doses of Arnica C30 taken in the 24 h postoperatively, and then three doses each day for 5 days postoperatively starting on the morning after the operation	Placebo	Infection rate (need for the prescription of systemic antibiotics)	No significant difference
				Median time spent in hospital	No significant difference
				Pain at 2-week follow up as measured by VAS	No significant difference
				Analgesic intake	No significant difference
				Mean pain score over 5 days as measured by VAS	No significant difference

Abbreviations: EL, Evidence level; SIGN, Scottish Intercollegiate Guidelines Network; VAS, Visual Analogue Scale.
[a] Level of evidence as assessed by the evidence reviewer.
[b] Study quality as assessed by the evidence reviewer using the methodology checklists developed by SIGN. An evidence level of '1' represents systematic reviews of RCTs or individual RCTs. An evidence level of '2' represents systematic reviews of case-control or cohort studies, or individual case-control or cohort studies. Quality ratings are based on an assessment of study design and risk of bias and are coded as '++', '+' or '-'. Studies of good quality are rated as '++', whilst poor quality studies are rated '-'.

2.2.8 Tracheal secretions

One Level II study (Frass et al, 2005; SIGN Evidence Level 1-) was identified that assessed the influence of sublingually administered homeopathic potassium dichromate C30 on the amount of

tenacious, stringy tracheal secretions in critically ill patients with a history of tobacco use and chronic obstructive pulmonary disease, compared with placebo (**Table 9**). This clinical condition was not included in the Overview Report as there were no relevant systematic reviews. Frass et al (2005) was a double-blind, placebo-controlled Level II study of 55 participants that found a significant effect of homeopathy in most of the reported outcomes. Tracheal secretions on day 2 were significantly reduced in the homeopathy group, compared with placebo ($p<0.0001$). Extubation could also be performed significantly earlier in the homeopathy group ($p<0.0001$) and the length of stay in intensive care was significantly shorter in the homeopathy group ($p<0.0001$). Consequently, the authors concluded that "these data suggest that potentised (diluted and vigorously shaken) potassium dichromate may help to decrease the amount of stringy tracheal secretions in chronic obstructive pulmonary disease patients".

The evidence reviewer notes that the Level II study by Frass et al (2005) had an appropriate method of allocation concealment and randomisation of subjects to treatment groups. However, there was a high risk of measurement bias in the study as a crucial limitation that was not addressed by the authors was whether or not the patients remained on any other medications during the trial period. It is thus unclear if the only difference between groups is the treatment under investigation which may have affected the outcomes. In addition, given that the study lasted 18 months, the evidence reviewer is cautious that only results of tracheal secretions at days 1 and 2 of treatment are presented. The findings by Frass et al (2005) cannot be interpreted further as the study is a self-selected sample and other literature concerning the effectiveness of homeopathy for tracheal sections has not been systematically retrieved.

Table 9 Evidence summary table of Frass et al (2005) on the effectiveness of homeopathy for the treatment of tracheal secretions

Study ID Level of evidence[a] *Quality*[b]	Patient population	Intervention	Comparator	Outcome	Results
Frass et al (2005) [Level II] *SIGN EL 1-* N=55	Critically ill patients with a history of tobacco use and chronic obstructive pulmonary disease	Potassium dichromate C30, 5 globules administered twice daily at intervals of 12 hours	Placebo	Tracheal secretions on day 1	No significant difference
				Tracheal secretions on day 2	Significantly reduced in favour of homeopathy (p<0.0001) • Homeopathy: 1.52±0.59 mL • Placebo: 2.44±0.65 mL
				Extubation	Could be performed significantly earlier in homeopathy group (p<0.0001) • Homeopathy: 2.88±1.20 days • Placebo: 6.12±3.13 days
				Length of stay in intensive care unit	Significant difference in favour of homeopathy (p<0.0001) • Homeopathy: 4.20±1.61 days • Placebo: 7.68±3.60 days

Abbreviations: C, Centesimal scale; EL, Evidence level; SIGN, Scottish Intercollegiate Guidelines Network.

[a] Level of evidence as assessed by the evidence reviewer.

[b] Study quality as assessed by the evidence reviewer using the methodology checklists developed by SIGN. An evidence level of '1' represents systematic reviews of RCTs or individual RCTs. An evidence level of '2' represents systematic reviews of case-control or cohort studies, or individual case-control or cohort studies. Quality ratings are based on an assessment of study design and risk of bias and are coded as '++', '+' or '-'. Studies of good quality are rated as '++', whilst poor quality studies are rated '-'.

2.2.9 Wound healing after foot surgery

One Level II study (Karow et al, 2008; SIGN Evidence Level 1-) was identified that aimed to determine if homeopathic *Arnica* D4 was as efficacious as diclofenac in relation to symptoms and wound healing after foot surgery (**Table 10**). This clinical condition was not included in the Overview Report as there were no relevant systematic reviews. Karow et al (2008) was a double-blind Level II study of 88 participants which found that *Arnica* D4 and diclofenac were equivalent for wound irritation and not therapeutically inferior to diclofenac for patient mobility. However, *Arnica* D4 was inferior to diclofenac with respect to pain. No significant differences between the two groups were found regarding the use of additional analgesics during the 4 postoperative days, though *Arnica* D4 was significantly better tolerated than diclofenac (p=0.049). In conclusion, the authors stated that "*Arnica* D4 can be used instead of diclofenac to reduce wound irritation".

The evidence reviewer notes that the Level II study by Karow et al (2008) utilised an appropriate method of randomisation and allocation concealment. However, a high risk of selection bias was present in the study. Patient demographics were not provided in the study and it was not mentioned if the study groups were comparable at baseline. It is also unclear if the patients remained on any other medications that may have influenced the outcomes. Loss to follow up was higher in the comparator group (20%; 9/44 participants) in comparison to the homeopathy group (5%; 2/44 participants) and the analysis was performed by per-protocol analysis instead of intention-to-treat. It is also not specified if the study was sufficiently powered to detect equivalence or non-inferiority. The findings by Karow et al (2008) cannot be interpreted further as the study is a self-selected sample and other literature concerning the effectiveness of homeopathy for wound healing after surgery has not been systematically retrieved.

Table 10 Evidence summary table of Karow et al (2008) on the effectiveness of homeopathy for wound healing after foot surgery

Study ID Level of evidence[a] *Quality*[b]	Patient population	Intervention	Comparator	Outcome	Results
Karow et al (2008) [Level II] *SIGN EL 1-* N=88	Men and women between the ages of 20 and 65 years with the surgical indication "Hallux valgus" or "Hallux rigidus" on the left and/or right metatarsa	Arnica D4, 10 pillules taken orally 3 times per day for 4 days postoperatively	Diclofenac sodium, 50 mg taken orally 3 times per day for 4 days postoperatively	Postoperative wound irritation – rubor by VAS	Arnica D3 and diclofenac are therapeutically equivalent Lower margin of the 95% CI on day 4 is 0.4729; p=0.049
				Postoperative wound irritation – swelling by VAS	Arnica D3 and diclofenac are therapeutically equivalent Lower margin of the 95% CI on day 4 is 0.3674; p=0.58
				Postoperative wound irritation – calor by VAS	Arnica D3 and diclofenac are therapeutically equivalent Lower margin of the 95% CI on day 4 is 0.4106; p=0.89
				Patient mobility (as measured by patient questionnaire on how long he/she had been out of bed)	Arnica D4 is not therapeutically inferior to diclofenac Lower margin of the 95% CI on day 4 is 0.4726; p=0.045
				Pain as calculated by an area under the curve	Arnica D4 is therapeutically inferior to diclofenac Lower margin of the 95% CI on day 4 is 0.2662; p=0.02
				Use of analgesics (Dipidolor, Tramal, Novalgin)	No significant difference
				Intolerance	Significant difference in favour of homeopathy (p=0.049) • Homeopathy group: 2/44 (4.5%) • Comparator group: 9/44 patients (20.45%)

Abbreviations: CI, Confidence interval; D, Decimal scale; EL, Evidence level; SIGN, Scottish Intercollegiate Guidelines Network; VAS, Visual Analogue Scale.

[a] Level of evidence as assessed by the evidence reviewer.

[b] Study quality as assessed by the evidence reviewer using the methodology checklists developed by SIGN. An evidence level of '1' represents systematic reviews of RCTs or individual RCTs. An evidence level of '2' represents systematic reviews of case-control or cohort studies, or individual case-control or cohort studies. Quality ratings are based on an assessment of study design and risk of bias and are coded as '++', '+' or '-'. Studies of good quality are rated as '++', whilst poor quality studies are rated '-'.

3 References

Linde K, Melchart D (1998) Randomized controlled trials of individualized homeopathy: a state-of-the-art review. J Altern Complement Med 4(4):371-88.

Myers CD, White BA, Heft MW (2002) A review of complementary and alternative medicine use for treating chronic facial pain. J Am Dent Assoc 133(9):1189-96.

NHMRC (2009). NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. National Health and Medical Research Council, Canberra ACT. Available at: https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf

Quinn F, Hughes C, Baxter GD (2006). Complementary and alternative medicine in the treatment of low back pain: a systematic review. Phys Ther Rev 11:107-116.

Raak C, Bussing A, Gassmann G, Boehm K, Ostermann T (2012) A systematic review and meta-analysis on the use of Hypericum perforatum (St. John's Wort) for pain conditions in dental practice. Homeopathy 101(4):204-10.

Roberts M, Brodribb W, Mitchell G (2012) Reducing the Pain: A Systematic Review of Postdischarge Analgesia Following Elective Orthopedic Surgery. Pain Med 13(5):711-27.

SIGN 50: A guideline developer's handbook (2011). Scottish Intercollegiate Guidelines Network. Available at: http://www.sign.ac.uk/guidelines/fulltext/50/index.html. Individual checklists available at: http://www.sign.ac.uk/methodology/checklists.html

Appendix A List of excluded studies

Reference	Level of evidence	Reason for exclusion
Adler, M. (1999). Efficacy, safety of a fixed-combination homeopathic therapy for sinusitis. *Adv. Ther.,* 16: 103-111.	Unable to assign a level of evidence - narrative review	Full text review. Excluded. Wrong research type or publication type
Aguejouf, O., Eizayaga, F.X., Desplat,V., Belon, P., Doutrempuich, C. Prothrombotic and haemorrhagic effects of aspirin. (2008). *Clinical Appl Thrombosis/Hemostas*; doi:10.1177/1076029608319945.	Unable to assign a level of evidence - in vitro study	Excluded. Study not published in the English language
Altman, D.G., Moher, D., Egger, M., Davidoff, F., Gotzsche, P.C. & Lang, T. (2001). The revised CONSORT statement for reporting randomised trials: explanation and elaboration. *Annals of Internal Medicine,* Vol. 134, pp.663-694.	Unable to assign a level of evidence - explanation of CONSORT statement	Excluded. Wrong research type or publication type
Altunç, U, Pittler, MH, Ernst, E. (2007). Homeopathy for childhood and adolescence ailments: systematic review of randomized clinical trials. *Mayo Clinic Proceedings*, 82: 69-75.	Level I	Systematic review included in Overview Report
Andersen, H.E, Eldov, P. (1999). Klassisk homøopati - og dens brugere. Institut for Samfundsfarmaci, Danmarks Farmaceutiske Højskole. 1995. In: Andersen, *Helle Egebjerg. En undersøgelse af Klassisk Homøpati. Teorier, praksis og brugererfaringer.* ISBN 87-987279-0-7	Unable to assign a level of evidence - not in English	Excluded. Study not published in the English language
Attena, F. et al (2000). Homeopathy in Primary Care: self reported change in health status. *Complementary therapies in Medicine;* Vol. 8: 1.	Level III-3	Excluded. Wrong research type or publication type
Aulas, J.J. & Chefdeville, F. (1984). A study of the history and critique of the sources of the homoeopathic materia medica: The origins and development of the Hahnemannian materia medica. Encycl. Med. Chir. Homoeopathie, 38080 (A10)	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Bailey, P. (1995). Homeopathic psychology. Kandern: Narayana Publications.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Bailey, P. (2010). Lac remedies in practice. Haarlem: Emryss.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Banerji, A. et al (2010). Chelidonium majus 30C and 200C in induced hepato-toxicity in rats. *Homeopathy,* Vol. 99:167-176	Unable to assign a level of evidence - animal study	Excluded. Non-human study
Barnes, J., Resch, K.L., & Ernst, E. (1997). H*omoeopathy for postoperative ileus*? A meta-analysis. Journal of Clinical Gastroenterology, 25: 628-633.	Level I	Systematic review included in Overview Report
Barry, CA (2006) The role of evidence in alternative medicine: Contrasting biomedical and anthropological approaches. Social Science and Medicine 62: 2646-2657	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Beauchamp, T. & Childress, J. (2001). *Principles of Biomedical Ethics,* 5th Ed, Oxford: Oxford University Press.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Behi, R, Nolan M. (1996). Quasi-experimental research designs. *British Journal of Nursing*, 5: 1079-1081.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Bell IR, Koithan M, (2012) A model for homeopathic remedy effects: low dose nanoparticles, allostatic cross-adaptation, and time-dependent sensitization in a complex adaptive system, *BMC Complementary and Alternative Medicine*, 12:191 doi:10.1186/1472-6882-12-191	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Bell IR, Lewis II DA, Brooks AJ, et al (2003) Gas discharge visualisation evaluation of ultramolecular doses of homeopathic medicines under blinded, controlled conditions. J Altern Complement Med 2003; 9: 25-38	Unable to assign a level of evidence - animal study	Excluded. Non-human study
Bell IR, Lewis II DA, Brooks AJ, Schwartz GE, Lewis SE, Walsh BT, Baldwin CM (2004) Improved clinical status in fibromyalgia patients treated with individualized homeopathic remedies versus placebo. Rheumatology 43: 577-582	Level II	Study included within a systematic review in the Overview Report
Bell, I.R. Lewis, D.A. 2nd, Brooks, A.J. et al 2004. Improved clinical status in fibromyalgia patients treated with individualized homeopathic remedies versus placebo. *Rheumatology*, 43: 577-582.	Level II	Study included within a systematic review in the Overview Report
Bellavite P, Ortolani R, Pontarollo F et al (2006) Immunology and homeopathy. 4. Clinical Studies - part 2.	Level I	Systematic review excluded from Overview Report - superseded publication
Bellavite P, Ortolani R, Pontarollo F. (2006). Immunology and homeopathy. 4. Clinical studies—Part 2. *Evidence-based Complementary and Alternative Medicine: eCAM*, 3: 397-409.	Level I	Systematic review included in Overview Report
Bellavite, P. & Signorini, A. (1995). *Homoeopathy: A frontier of medical science.* Berkeley, North Atlantic Books.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Belon P, Cumps J, Ennis M et al (2004) Histamine dilutions modulate basophil activation. Inflammation Research 53: 181-188	Unable to assign a level of evidence - in vitro study	Excluded. Wrong research type or publication type
Belon, P. Cumps, J. Ennis, M., Mannaioni, P.F. Roberfroid, M. Saint-Laudy, J. Weigart, F.A.C. (2004). *Histamine dilutions modulate basophil activity*. *Inflamm. Res;* 53: 181-188.	Unable to assign a level of evidence - in vitro study	Excluded. Wrong research type or publication type
Benveniste, J. (1981). *Human basophil degranulation test as an in-vitro method for the diagnosis of allergy*. Clin Allergy 11:1.	Unable to assign a level of evidence - in vitro study	Excluded. Wrong research type or publication type
Betti, L. Brizzi, M. Nani, D. Peruzzi, M. (1997). *Effects of high dilutions of Arsenicum Album on wheat seedlings on seeds poisoned with the same substance*. *Br Hom J* ; 86:86-89.	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Boissel, J.P., Cucherat, M, Haugh, M. Gauthier, E. (1996). Critical literature review on the effectiveness of homoeopathy: overview of data from homoeopathic medicine trials. In: *Homoeopathic Medicine Research Group, Report of the Commission of the European Communities, Directorate-General XII—Science, Research and Development, Directorate E—RTD Actions: Life Sciences and Technologies*—Medical Research, Brussels, Belgium.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Bond, R.A. (2001). Is paradoxical pharmacology a strategy worth pursuing? *Trends in pharmacological Sciences* 22:273-276.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Booth, A. (2009). What proportion of healthcare is evidence-based? Resource Guide NHS items studied in UK . Available at: http://www.shef.ac.uk/scharr/ir/percent.html#genmed	Unable to assign a level of evidence - literature/narrative review	Excluded. Wrong research type or publication type
Bordet, MF, Colas, A, Marijnen P, et al (2008). Treating hot flushes in menopausal women with homeopathic treatment—results of an observational study. *Homeopathy*, 97: 10-15.	Level III-3	Excluded. Wrong research type or publication type
Bornhöft, G., Wolf, U., Ammon, K., et al 2006. Effectiveness, safety and cost-effectiveness of homeopathy in general practice—summarized health technology assessment. *Forschende Komplementärmedizin*, 13 (Suppl 2): 19-29	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Boulderstone J (2009) Memorandum	Unable to assign a level of evidence - memorandum	Excluded. Wrong research type or publication type
Brach, A, Strube J, Stolz P, Decker H. (2001). Effects of ultrahigh *Vibrio fischeri*. Biochim Biophys Acta: 1621: 253-60.	Unable to assign a level of evidence - in vitro study	Excluded. Wrong research type or publication type
Bracho G et al (2010) Large-scale application of highly -diluted bacteria for Leptospirosis epidemic control. Homeopathy 99: 156-166	Not applicable. Out of scope	Excluded. Out of scope - homeopathy for prophylactic use
Bradford, T. L. (2004). *Life and letters of Dr. Samuel Hahnemann.* New Delhi: B. Jain Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Brien S, Lachance L, Prescott P, McDermott C, Lewith G (2011) 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* **50:** 1070-1082	Not applicable. Out of scope	Full text review. Excluded. Out of scope - homeopathy used in conjunction with other therapies where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)
Brinkaus, B. (2006). Homeopathic Arnica therapy in patients receiving knee surgery: results of three randomised double-blind trials. Comp Ther Med 14: 237-246.	Level II	Study included within a systematic review in the Overview Report
British Homoeopathic Association: www.britishhomeopathic.org/research/science_and_technology_committee_report.html	Unable to assign a level of evidence - description of UK "Evidence check on homeopathy"	Excluded. Wrong research type or publication type
Calabrese, E. J. Staudenmayer, J. Stanek E. J. (2006a). Drug development and hormesis. Changing conceptual understanding of the dose response creates new challenges and opportunities for more effective drugs. *Curr. Opin. Drug Discov. Devel.* 9, 117-123.	Unable to assign a level of evidence - literature/narrative review	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Calabrese, E. J., Blain, R. (2005). The occurrence of hormetic dose responses in the toxicological literature, the hormesis database: An overview. *Toxicol. Appl. Pharmacol.* 202, 289-301.	Unable to assign a level of evidence - overview of hormesis database	Excluded. Wrong research type or publication type
Calabrese, E.J, Bachmann, K.A. Bailer, A.J. et al. (2007). Biological stress response terminology: Integrating the concepts of adaptive response and preconditioning stress within a hormetic dose-response framework. *Toxicol Appl Pharmacol.,* 222: 122-128.	Unable to assign a level of evidence - recommendations	Excluded. Wrong research type or publication type
Calabrese, E.J. Staudenmayer, J.W., Stanek, E.J., Hoffmann, G.R. (2006b). Hormesis Outperforms Threshold Model in National Cancer Institute Antitumor Drug Screening Database. *Toxicol Sci* 2006:94;368-378	Unable to assign a level of evidence - not an intervention study	Excluded. Wrong research type or publication type
Chatfield, K., & Relton, C. (2005). Are the effects of homoeopathy placebo effects? – A full critique of the article by Shang et al, 2005. www.homeopathycourses.com/lancet.html	Unable to assign a level of evidence - critique of systematic review	Excluded. Wrong research type or publication type
Chirumbolo, S., Brizzi M., Ortolani, R., Vella, A., Bellavite, P. (2009). Inhibition of CD203c membrane upregulation in human basolphils by high dilutions of histamine: a controlled replication study. *Inflam Res.* 2009: DOI 10.1007/s00011-009-0044-4	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Christie, E.A. & Ward, A.T. (1996). Report on NHS practice-based homoeopathy project. Analysis of effectiveness and cost of homoeopathic treatment within a GP practice at St. Margaret's Surgery, Bradford on Avon,Wilts. *The Society of Homeopaths*. ISBH 1 901262 006.	Level IV	Excluded. Wrong research type or publication type
Clover, A. (2000). A patient benefit survey: Tunbridge Wells Homoeopathic Hospital. *British Homeopath J*, 89: 68-72	Level IV	Excluded. Wrong research type or publication type
Coulter, H. (1973). *Divided legacy: the conflict between homoeopathy and the American Medical Association.* Berkeley: North Atlantic Books.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Coulter, M.K., Dean, M.E. (2007). Homeopathy for attention deficit/hyperactivity disorder or hyperkinetic disorder *(Cochrane Review)*. In: The Cochrane Library. Chichester, UK: John Wiley & Sons, Ltd. CD005648.	Level I	Systematic review excluded from Overview Report - superseded publication
Cucherat, M. & Linde, K. (2000). Evidence of clinical effectiveness of homeopathy: a meta-analysis of clinical trials. *Eur J Clin Pharmacol* 56: 27-33.	Level I	Systematic review included in Overview Report
Dangouman, J. (1996). In: *Homoeopathic Medicine Research Group Report,* Homoeopathic Medicine Research Group Report, Brussels, p. 211-229.	Unable to assign a level of evidence - report	Excluded. Wrong research type or publication type
Dantas (2005) untitled. *The Lancet* **366:** 2083-2085	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type
Dantas, F. & Fisher, P. (1998). A systematic review of homoeopathic pathogenetic trials ('provings') published in the United Kingdom from 1945-1995. In: E. Ernst & E.G. Kahn (Eds.) *Homoeopathy: a critical appraisal,* pp. 69-97. London: Butterworth Heinemann.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Dantas, F. & Rampes, H. (2000). Do Homeopathic Medicines Provoke Adverse Effects? A Systematic Review. *British Homeopathic Journal*; 89: 70-74.	Level I	Excluded. Wrong research type or publication type
de Oliveira, C.C., de Oliviera, S.M., Goes, V.M., Probst, C.M., Kreiger, M.A., Buchi, D.D. (2008). Gene expression profiling in macrophages following mice treatment with an immunomodulatory medication. J Cell Biochem.,104:1364-1377.	Unable to assign a level of evidence - animal study	Excluded. Wrong research type or publication type
Dean, M.E. (2004). *The trials of homoeopathy: origins, structure and development.* Essen: KVC.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Dempster, A. (1997). *Homoeopathy within the NHS. Evaluation of homoeopathic treatment of common mental health problems. 1995 - 1997.* Rydings Hall Surgery, Brighouse, West Yorkshire. ISBN No 1901262014.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Devenas, E., Beauvais, F. Amara, J., Oberbaum, Robinson, B., Miadonna,A., Tedesci, A., Pomeranz, B., Fortner, Belon, Saint-Laudy, J., Poitevin, B. & Benveniste, J. (1988). Human basophil degranulation triggered by very dilute anti-serum against IgE. Nature: 366: 816-818.	Unable to determine level of evidence - narrative review	Excluded. Wrong research type or publication type
Diefenbach M, Schilken J, Steiner G, Becker HJ. Homeopathic therapy in respiratory tract diseases. Evaluation of a clinical study in 258 patients. Z Allgemeinmed 1997; 73; 308-14	Level II	Study included within a systematic review in the Overview Report
Dimitriades, G. (2004). *Homoeopathic diagnosis: Hahnemann through Boenninghausen*. Kandern: Narayana Publications	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Dimitriades, G. (2005). *The theory of chronic diseases according to Hahnemann.* Kandern: Narayana Publications.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Dimpfel, W. (2010). How natural medications affect the brain. *European Journal of Integrative Medicine Issue* 2, 4:227 - 228.	Level IV	Excluded. Wrong research type or publication type
Diodge, N. 2007. *The brain that changes itself.* Melbourne: Scribe.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Dorsey ER, et. Al. 'Funding of US Biomedical Research, 2003-2008' JAMA 2010; 303 (2): 137-43	Unable to assign a level of evidence - review of US funding	Excluded. Wrong research type or publication type
Eizayaga, F.X., Aguejouf, O., Desplat, V., Doutremepuich, C. (2007). Modifications produced by indomethacin and L-NAME in the effect of ultrlow-dose aspirin on platelet activity in portal hypertension. *Pathophysiol Haemostasis Thrombosis*, 35:375-363.	Unable to assign a level of evidence - animal study	Excluded. Wrong research type or publication type
Elia, V. Niccoli, M. (1999). Thermodynamics of extremely diluted aqueous solutions. Ann NY Acad Sci., 879:241.	Unable to assign a level of evidence - thermodynamic study	Excluded. Wrong research type or publication type
Elia, V., Napoli, E., Niccoli, M., et al. (2004). New physicochemical properties of extremely diluted aqueous solutions: a calorimetric and conductivity study at 25IC. J Therm Anal Calorimetry, 78:331-342.	Unable to assign a level of evidence - physicochemical study	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Elia, V., Elia, L., Marchettini, N., Napoli, E., Niccoli, M., Tiezzi, E. (2008). Physicochemical properties of aqueous extremely diluted solutions in relation to aging. . J Therm Anal Calorimetry, 93:1003-1011.	Unable to assign a level of evidence - physicochemical study	Excluded. Wrong research type or publication type
Endler, P.C. & Schulte, J. (Eds) (2001). *Ultra high dilutions.* Dordrecht: Kluwer Acad. Publ.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Endler, P.C. Pongratz, W. van Wijk, R. Kastberger, G., Haidvogl, M. (1991). Effects of highly diluted succussed thyroxin on metamorphosis of highland frogs. Berlin J Res Hom., 1:151-160.	Unable to assign a level of evidence - animal study	Excluded. Wrong research type or publication type
ENHR: European Network of Homeopathy Researchers. (2006). An overview of positive homeopathy research and surveys. Available on the website of the *European Central Council of Homeopaths* - www.homeopathy-ecch.org	Unable to assign a level of evidence - summary of positive homeopathic research	Excluded. Wrong research type or publication type
Ernst E (2010) Homeopathy: What does the 'best' evidence tell us. Medical Journal of Australia 192: 458-460	Unable to assign a level of evidence - overview	Excluded. Wrong research type or publication type
Ernst E (2011) Homeopathy, non-specific effects and good medicine. *Rheumatology* **50:** 1007-1008	Unable to assign a level of evidence - editorial	Excluded. Wrong research type or publication type
Ernst, E. & Barnes, A. (1998). Are homeopathic remedies effective for delayed-onset muscle soreness? A systematic review of placebo controlled trials. *Perfusion,* 11: 4-8.	Level I	Systematic review included in Overview Report
Ernst, E. & Pittler, M.H. (1998). Efficacy of homoeopathic Arnica: a systematic review of placebo controlled clinical trials. *Archives of Surgery* 133: (11): 1187-90.	Level I	Systematic review included in Overview Report
Fanelli D (2009) How Many Scientists Fabricate and Falsify Research? A Systematic Review and Meta-Analysis of Survey Data. PLoS ONE 4 (5): e5738. DOI: 10.1271/journal.pone.0005738	Level I	Systematic review excluded from Overview Report - wrong intervention
Fimiani, V. Cavallaro, A. Ainis, O. Bottari, C. (2000). Immunomodulatory effect of the homoeopathic drug Engystol-N on some activities of isolated human leukocytes and in whole blood. *Immunopharmacol-Immunotoxicol,* 22:103-115.	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Fisher P, Greenwood A, Huskisson EC, Turner P, Belon P (1989) Effect of homoeopathic treatment on fibrositis (primary fibromyalgia) BMJ 299: 365-366	Level II	Study included within a systematic review in the Overview Report
Fisher, P. (2006). Homoeopathy and The Lancet Evidence-based complementary and alternative medicine. Available on line: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1375230/	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Fisher, P. (1986). An experimental double-blind clinical trial method in homoeopathy. Use of a limited range of remedies to treat fibrositis. *British Homeopathic Journal*, 75: 142-147.	Level II	Study included within a systematic review in the Overview Report
Fisher, P. (2007). The memory of water – a scientific heresy? *Homoeopathy,* 96 (3): 141-2.	Unable to assign a level of	Excluded. Wrong research type or

Reference	Level of evidence	Reason for exclusion
	evidence - editorial	publication type
Fisher, P. (2008a). Homoeopathic clinical trials. Proceedings of the *Australian Homoeopathic Association Conference, Sydney: AHA.*	Unable to assign a level of evidence - conference proceedings	Excluded. Wrong research type or publication type
Fisher, P. (2008b). Homoeopathy – evidence and efficacy. Proceedings of the *Australian Homoeopathic Association Conference*, Sydney: AHA.	Unable to assign a level of evidence - conference proceedings	Excluded. Wrong research type or publication type
Frass M, Linkesch M, Banyai S, Resch G, Dielacher C, Loebl T, Endler C, Haidvogl M, Muchitsch I, Schuster E. Adjunctive homeopathic treatment in patients with severe sepsis: A randomized, double-blined, placebo-controlled trial in an intensive care unit. *Homeopathy* **94:** 75-80	Not applicable. Out of scope	Full text review. Excluded. Out of scope - homeopathy used in conjunction with other therapies where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)
Frenkel M et al (2010) Cytotoxic effects of ultra-diluted remedies on breast cancer cells. International Journal of Oncology 36: 395-403	Unable to assign a level of evidence - in vitro study	Excluded. Wrong research type or publication type
Friese, K.H. Kruse, S. Ludtke, R. Moeller, H. (1997). Homeopathic treatment of otits media in children: comparisons with conventional therapy. *Int J Clin Pharmacol Ther;* 35: 296-301.	Level III-2	Study included within a systematic review in the Overview Report
Friese, K-H, Zabalotnyi, D.I. (2007). Homeopathy in acute rhinosinusitis. A double-blind, placebo controlled study shows the efficiency and tolerability of a homeopathic combination remedy. *HNO*, 55: 271-277.	Level II	Full text review. Excluded. Study not published in the English language
Fuller Royal, F. (1991). Proving homoeopathic medicines. *Brit. Hom. J.* 80:122.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Garrett, B, Harrison, PV, Stewart, T, Porter, I. 1997. A trial of homoeopathic treatment of leg ulcers. *Journal of Dermatological Treatment*, 8: 115-117. *(Reports results of two trials)*	Level I	Systematic review included in Overview Report
Ghosh, A. (1983). Homoeopathic treatment of osteoarthritis (letter). *Lancet* 1:304	Unable to assign a level of evidence - letter to the editor	Excluded. Wrong research type or publication type
Gibson, R.G., Gibson, S.L.M., MacNeill, A.D., Buchanan,W.W. (1980). Homoeopathic therapy on rheumatoid arthritis: evaluation of double-blind clinical therapeutic trial. British Journal of Clinical Pharmacology 9: 453-459.	Level II	Study included within a systematic review in the Overview Report
Goodman S, Greenland S (2007). Why Most Published Research Findings are False: problems in the Analysis .PLoS Med. April; 4 (4): e215. doi: 10.1371/journal.pmed.0040168	Unable to assign a level of evidence - literature/narrative review	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Gray, A. (2005a). *Experience of Medicine Vol.1*. Three provings by students of Nature Care College. Sydney: 70 meters & Nature Care College.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Gray, A. (2005b). *Experience of Medicine Vol. II*. Four Sydney: 70 meters & Nature Care College.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Gray, A. (2006a). *Experience of Medicine Vol. III.* Haarlem: Emryss Publishing	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Gray, A. (2006b). *Experience of Medicine Vol. IV*. Haarlem: Emryss Publishing	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Guedes, J.R.P., Ferriera, C.M., Guimaraes, H.M.B., Saldiva, P.H.N. Capelozzi, V.L. (2004). Homoeopathically prepared dilution of Rana catesbeiana: thyroid gland modifies its rate of metamorphosis. *Homoeopathy*, 93:132-137.	Unable to assign a level of evidence - animal study	Excluded. Non-human study
Guedes, JRP et al. Ultra High Dilution of triiodothyronine modifies cellular apoptosis in Rana catesbeiana tadpole tail in vitro. Homeopathy(2011)100, 220-27	Unable to assign a level of evidence - animal study	Excluded. Non-human study
Güthlin, C. Lange, O. and Walach, H. (2004). Measuring the effects of acupuncture and homoeopathy in general practice: An uncontrolled prospective documentation approach. *BMC Public Health;* 4:6.	Level IV	Excluded. Wrong research type or publication type
Haehl, R. (1995). *Samuel Hahnemann, his life and work.* New Delhi: B. Jain.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Hahnemann, S. (1970) *The organon of medicine, 6th edition.* New Delhi: Jain Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Haidvogl M et al (2007) Homeopathic and conventional treatment for acute respiratory and ear complaints: A comparative study on outcome in the primary care setting. BMC Complementary and Alternative Medicine 7	Level III-2	Study included within a systematic review in the Overview Report
Haidvogl, M. (1994). Clinical studies on homoeopathy. The problem of a useful design. In: P.C. Endler, & J. Schulte, (eds) *Ultra high dilutions.* Dordrecht: Kluwer Acad. Publ., p. 233.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Harrison, H. Fixsen, A. Vickers, A (1999). A randomized comparison of homoeopathic and standard care for the treatment of glue ear in children. *Complementary Therapies in Medicine*, 7: 132-135.	Level II	Study included within a systematic review in the Overview Report
Hart, O. Mullee, MA. Lewith, G. Miller, J. (1997). Double-blind, placebo-controlled, randomized clinical trial of homoeopathic arnica C30 for pain and infection after total abdominal hysterectomy. *Journal of the Royal Society of Medicine*, 90: 73-78.	Level II	Included
Hatherly, P. (2010). *The lacs: a materia medica and repertory*. AEN Publishers, Kenmore.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Heirs M, Dean ME. Homeopathy for attention deficit/hyperactivity disorder or hyperkinetic disorder. Cochrane Database of Systematic Reviews 2007, Issue 4. Art. No.: CD005648. DOI: 10.1002/14651858.CD005648.pub2	Level I	Systematic review included in Overview Report
Herrick, N. (2009). *Animal mind: human voices*. Arcata, CA: Whole Health Now.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Hill N, Stam C, Tuinder S, van Haselen RA (1995). A placebo controlled clinical trial investigating the efficacy of a homeopathic after-bite gel in reducing mosquito bite induced erythema. *European Journal of Clinical Pharmacology*, 49: 103-108.	Not applicable. Out of scope	Full text review. Excluded. Out of scope - homeopathy used in conjunction with other therapies where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)
Hill N, Stam C, van Haselen RA (1996). The efficacy of Prrrikweg gel in the treatment of insect bites: a double-blind, placebo-controlled clinical trial. *Pharmacy World and Science*, 18: 35-41.	Not applicable. Out of scope	Full text review. Excluded. Out of scope - homeopathy used in conjunction with other therapies where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)
Homoeopathic Research Institute: principals: Dr Alexander Tournier PhD., Clare Relton MSc., Dr Robert Mathie PhD., Dr Elizabeth Thompson BAOxon MBBS MRCP FFHom., Prof. Kate Thomas, Dr Lionel Milgrom PhD., Dr Mike Emmans Dean Ph.D., Dr Nagin Lad PhD., Dr Natasha Peric-Concha PhD.,Dr Patti Bayliss MB., ChB FRCGP www.homeoinst.org/document-archive	Unable to assign a level of evidence - website	Excluded. Wrong research type or publication type
Hornung, J. & Vogler, S. (1990). A documentation project. Clinical studies in unconventional treatment in cancer.Berlin J. Research Homoeopathy.1: 22.	Unable to assign a level of evidence - website	Excluded. Wrong research type or publication type
Hornung, J. (1991). An overview of the formal methodology requirements for controlled clinical trials. *Berlin J. Res. Homoeopathy.* Vol. 1, pp. 288-97	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
House of Commons 2010 *The House of Commons Science and Technology Committee Evidence Check 2: Homoeopathy. Fourth Report of the Session* 2009-20 London: The Stationery Office Limited	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Ioannidis JPA (2005) Why most published research findings are false. PLoS Medicine 2: 696-701	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type
Ionnadis JPA (2007) Why Most Published Research Findings are False: Author's Reply to Goodman and Greenland. PLoS Med. June 4 (6): e215 doi: 10.1371/journal.pmed.0040215	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Jacobs, J. et al, (2001). Homoeopathic treatment of acute otitis media in children: a preliminary randomised placebo-controlled trial. *Pediatr Infect Dis Journal*: 20: 177-183	Level II	Study included within a systematic review in the Overview Report
Jacobs, J. Herman, P. Heron, K. (2005). Homoeopathy for menopausal symptoms in breast cancer survivors: a preliminary randomised controlled trial. *J Alt Comp Med.,*11:21-27.	Level II	Study included within a systematic review in the Overview Report
Jacobs, J. Jonas, W.B. Jimenez-Perez, M. Crothers, D. (2003). Homeopathy for childhood diarrhea: combined results and metaanalysis from three randomized, controlled clinical trials. *Pediatric Infectious Disease Journal*, 22: 229-234.	Unable to assign a level of evidence - non-systematic review	Excluded. Wrong research type or publication type
Jacobs, J., Springer, D.A., Crothers, D. 2001. Homoeopathic treatment of acute otitis media in children: a preliminary randomises placebo-controlled trial. *Pediatr Infect Dis J.,* 20: 177-183.	Level II	Study included within a systematic review in the Overview Report
Jadad, A., Moore, R.A., Carroll, D., Jenkinson, C., Reynolds D.J.M., Gavaghan D.J., McQuay H.J. 1996. "Assessing the quality of reports of randomized clinical trials: Is blinding necessary?" *Controlled Clinical Trials* 17 (1): 1–12	Unable to assign a level of evidence - protocol	Excluded. Wrong research type or publication type
Jain, A. (2003). Does homoeopathy reduce the cost of conventional drug prescribing? A study of comparative drug prescribing costs in general practice. *Homoeopathy*; 92: 71-76.	Unable to assign a level of evidence - economic study	Excluded. Wrong research type or publication type
Johannessen, T., Fossvedt, D., & Petersen, H. (1991). Combined single subject trials. *Scandinavian Journal Of Primary Health Care*, Vol. 9, pp. 23-27.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Jonas, W.B. (2003). A critical overview of homoeopathy. *Ann Int Med* 138: 393-399.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Jonas, W.B. Ives, J.A. Rollwagen, F. (2006). Can specific biological signals be digitized? *FASEB J* Vol. 20:23–28.	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Jonas, W.B., Linde, K, Ramirez, G. (2000). Homeopathy and rheumatic disease. *Rheumatic Disease Clinics of North America*, 26: 117-123.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Kainz, J.T. Kozel, G. Haidvogl, M. Smolle, J. (1996). Homoeopathic versus placebo therapy of children with warts on the hands: a randomized, double-blind clinicaltrial. *Dermatology*, 193: 318-320.	Level II	Study included within a systematic review in the Overview Report
Kassab S, Cummings M, Berkovitz S, van Haselen R, Fisher P. Homeopathic medicines for adverse effects of cancer treatments. Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD004845. DOI: 10.1002/14651858.CD004845.pub2	Level I	Systematic review included in Overview Report
Kassab, S. Cummings, M. Berkovitz, S. et al (2009). Homeopathic medicines for adverse effects of cancer treatments *(Cochrane Review)*. In: The Cochrane Library. Chichester, UK: John Wiley & Sons, Ltd. CD 004845.	Level I	Systematic review included in Overview Report

Reference	Level of evidence	Reason for exclusion
Kaziro GS (1984). Metronidazole (Flagyl) and Arnica montana in the prevention of post-surgical complications, a comparative placebo controlled clinical trial. Britis*h Journal of Oral & Maxillofacial Surgery*, 22: 42-49.	Not applicable. Out of scope	Full text review. Excluded. Out of scope - homeopathy used in conjunction with other therapies where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)
Keil, T. Witt, C .M. Roll S. Vance, W. Weber, K. Wegscheider, K, Willich, S. N. (2008). Homoeopathic versus conventional treatment of children with eczema: A comparative cohort study. *Complementary Therapies in Medicine*, 16:15-21.	Level III-2	Study included within a systematic review in the Overview Report
Kennedy, C. 1971 A controlled trial. *British Homoeoapthic Journal,* Vol. 60, 120-127.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Kleijnen J, Knipschild P, ter Riet G (1991) Clinical trials of homoeopathy. BMJ 302: 316-323	Unable to assign a level of evidence - non-systematic review	Excluded. Wrong research type or publication type
Kleijnen, J, Knipschild, P., ter Reit, G. (1991). Clinical trials in homoeopathy. *British Medical Journal,* 302:316-323.	Unable to assign a level of evidence - non-systematic review	Excluded. Wrong research type or publication type
Klein, L. (2009). *The miasms and nosodes – origins of disease.* Vol. 1. Kandern: Narayana Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Klopp, R, Niemer, W. & Weiser M. (2005). Microcirculatory effects of a homeopathic preparation in patients with mild vertigo: an intravital microscopic study. *Microvascular Research*, 69: 10-16.	Not applicable. Out of scope	Full text review. Excluded. Out of scope - homeopathy used in conjunction with other therapies where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)
Labrecque M, Audet D, Latulippe LG, Drouin J (1992). Homoeopathic treatment of plantar warts. *Canadian Medical Association Journal*, 146: 1749-1753.	Level II	Study included within a systematic review in the Overview Report
Le Roux, P. (2005). *The Metals in Homoeopathy: core essences and paediatric cases for all of the elements of the iron, silver and gold series*. Kandern: Narayana Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Le Schepper, L. (2009). *Achieving and maintaining the similimum*. Kandern: Narayana Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Le Schepper, L. (2010). *Hahnemann Re-visited: a textbook of classical homoeopathy for the professional.* Kandern: Narayana Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Lelannne, M., Doutremepuich, C., De Seze, O., Belon, P. (1990). What is the effect of acetylsalicylic acid at ultralow dose on the interaction of platelets/vessel wall? *Thrombosis Res.,* 60:231-236.	Unable to assign a level of evidence - in vitro study	Excluded. Wrong research type or publication type
Levy, D. (2008). Enhancing professional efficacy through the application of clinical auditing and reflective practice. In: *Proceedings of the Australian Homoeopathic Medicine Conference*, Sydney: AHA publication. (www.homeopathynsw.org)	Unable to assign a level of evidence - conference proceedings	Excluded. Wrong research type or publication type
Lin, V. Bensoussan, A. Myers, S.P., McCabe, P., Cohen, M. Hill, S. & Howse, G. (2005). The practice and regulatory requirements of naturopathy and western herbal medicine. School of Public Health: Latrobe University. www.health.vic.gov.au/pracreg/naturopathy.htm	Unable to assign a level of evidence - government report	Excluded. Wrong research type or publication type
Linde K, Jonas W (2005) Are the clinical effects of homoeopathy placebo effects. *The Lancet* **366:** 2081-2082	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type
Linde K. Jonas WB, Melchart D, Worku F, Wager H, Eital F, Critical Review and Meta-Analysis of Serial Agitated Dilutions in Experimental Toxicology. Human and Experimental Toxicolgy. 1994; 13: 481-492.	Level I	Excluded. Wrong intervention
Linde, K. & Melchart, D. (1998). Randomised controlled trials of individualised homeopathy: a state-of-the-art review. Journal of Alternative and Complementary Medicine 4: 371-388.	Level I	Systematic review included in Overview Report
Linde, K. Scholz, M. Ramirez, G., Clausius, N. Melchart, D. & Jonas, W.B. (1999). Impact of study quality on outcomes in placebo-controlled trials of homoeopathy. *Journal of Clinical Epidemiology* 52: 631-636.	Level I	Systematic review excluded from Overview Report - wrong outcomes
Linde, K., Clausius, N., Ramirez, G., Melchart, D., Eitel, F., Hedges, L.V. & & Jonas, W.B. (1997). Are the clinical effects of homoeopathy placebo effects? A meta-analysis of placebo controlled trials. Lancet, 350: 834-843.	Level I	Systematic review included in Overview Report
Lökken, P. Straumsheim, P.A, Tveiten D, et al (1995). Effect of homoeopathy on pain and other events after acute trauma; placebo controlled trial with bilateral oral surgery. *British Medical Journal*, 310: 1439-1442.	Level II	Study included within a systematic review in the Overview Report
Long, L. & Ernst, E. (2001). Homeopathic remedies for the treatment of osteoarthritis: a systematic review. *British Homeopathic Journal*, 90: 37-43.	Level I	Systematic review included in Overview Report
Lorenz, I., Schneider, E.M., Stolz, P., Brack, A. & Strube, J. (2003). Sensitive flow cytometric method to test basophil activation influenced by homeopathic histamine dilutions. *Forsch Komplementarmed Klass Naturheilkd*; 10(6): 316-24.	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Lüdtke R, Rutten ALB (2008) The conclusions on the effectiveness of homeopathy highly depend on the set of analyzed trials. *Journal of Clinical Epidemiology* **61:** 1197-1204	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Lüdtke R, Rutten ALB (2008) The conclusions on the effectiveness of homeopathy highly depend on the set of analyzed trials. Journal of Clinical Epidemiology 61: 1197-1204	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Ludtke, R. & Rutten, A.L. (2008). The conclusions on the effectiveness of homeopathy highly depend on the set of analysed trials. *Journal of Clinical Epidemiology,* 61(12):1197-204.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Ludtke, R. & Stolper, C.F. (2008). The 2005 meta-analysis of homeopathy: the importance of post-publication data. *Homoeopathy,* Vol. 97:169-77.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Ludtke, R. & Wilkins, R. (1999). Clinical trials of Arnica in homoeopathic preparations. In: Albrecht, H. Fruhwald, M. (eds) *Jahrbuch*. Carl & Veronica Carstens-Stiftung. KVC Verlag: Essen pp. 97-112.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Ludtke, R. et al, (2009). In: *New directions in homoeopathic research,* Witt, J., & Albrecht, H. eds. Kandern: Narayana publications.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Mangialavori, M. (2005). *Praxis - method of complexity: the search for coherence in clinical phenomena* Volumes 1: Methodology. Modena: Matrix.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Mangialavori, M. (2003). *Homoeopathy for anger and mortification*. Kandern: Narayana publications.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Mangialavori, M. (2004). *Solanaceae.* Kandern: Narayana publications.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Mangialavori, M. (2010). *Praxis Volume 2: Materia Medica*. Kandern: Narayana publications.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Mangialavori, M. (2010). *Self destructiveness – The acids and similars in homoeopathic medicine.* Kandern: Narayana publications.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Marks, B. & Twohig, J. (2000). *A Homeopathic Proving of Latrodectus Hasseltii Red Back Spider*. Minutus Homeopathy Books.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Martins de Oliveira, Simone et al. Mercurius solubilis: actions on macrophages. Homeopathy(2011)100, 228-36	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Master, F. (2007). *The web spinners.* New Delhi: Jain Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Mathie, R. (2003). The research base of homeopathy: a fresh assessment of the literature. *Homeopathy,* 92: 84-91.	Level I	Systematic review included in Overview Report
Mathie, R. (2010). Memorandum submitted by the British Homeopathic Association (HO 12). www.publications.parliament.uk/pa/cmselect/cmsctech/45/09112511.htm	Unable to assign a level of evidence - memorandum	Excluded. Wrong research type or publication type
McCarney RW, Linde K, Lasserson TJ. Homeopathy for chronic asthma. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.: CD000353. DOI: 10.1002/14651858.CD000353.pub2.	Level I	Systematic review included in Overview Report

Reference	Level of evidence	Reason for exclusion
McCarney RW, Warner J, Fisher P, van Haselen R. Homeopathy for dementia. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No.: CD003803. DOI: 10.1002/14651858.CD003803	Level I	Systematic review included in Overview Report
McCarney, R. Warner, J. Fisher, P. van Haselen, R. 2004 McCarney RW, Linde K, Lasserson TJ (2004). Homeopathy for chronic asthma *(Cochrane Review).* In: The Cochrane Library. Chichester, UK: John Wiley & Sons, Ltd. CD000353.	Level I	Systematic review included in Overview Report
McGauran N. et. Al. (2010) Reporting bias in medical research - a narrative review. Trials, 11:37. www.trialsjournal.com/content/11/1/27.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Medhurst, R. (2004). Homoeopathy around the world. *Journal of the Australian Traditional Medicine Society,* Vol. 10, no. 4.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Media article: Australian Broadcasting Commission (2009) The World Today 3.2.2009	Unable to assign a level of evidence - media article	Excluded. Wrong research type or publication type
Media article: Pharmaceutical Industry Hustlers - Part I SSRI Antidepressants Pushers (2008) Wordpress.com. 8.11.2008	Unable to assign a level of evidence - media article	Excluded. Wrong research type or publication type
Milazzo S, et al. *(*2006). Efficacy of homeopathic therapy in cancer treatment. *European Journal of Cancer***,** 42: 282-289.	Level I	Systematic review included in Overview Report
Milgrom L Chatfield K (?) "It's the consultation, stupid!" Isn't it? Word document - Pre-print of an article to be published in the Journal of Alternative and Complementary Medicine.	Unable to assign a level of evidence - editorial	Excluded. Wrong research type or publication type
Milgrom L Chatfield K (?) Against scientism - critique of a utilitarian perspective on homeopathy. Word doucment - Letter that will be appearing in Bioethics later this year.	Unable to assign a level of evidence - letter to the editor	Excluded. Wrong research type or publication type
Moher, D., Cook, D.J., Eastwood, S., Olkin, I., Rennie, D., Stroup, D.F. (1999). Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement: The quality of reporting of meta-analyses. *The Lancet,* 354:1896-900.	Unable to assign a level of evidence - conference proceedings	Excluded. Wrong research type or publication type
Moher, D., Jones, A., Cook, D., Jadad, A.R., Moher, M., Tugwell, P. & Klassen, T. (1998). Does the quality of reports of randomized trial affect estimates of intervention efficacy reported in meta-analyses? *The Lancet,* Vol. 352, pp. 609-613.	Unable to assign a level fo evidence - non systematic review	Excluded. Wrong research type or publication type
Möllinger H, Schneider R, Walach H (2009) Homeopathic pathogenetic trials produce specific symptoms different from placebo. *Forschende Komplementärmedizin* **16:** 105-110	Level II	Full text review. Excluded. Wrong outcomes
Montagnier, L. et al. (2009). Electromagnetic signals are produced by aqueous nanostructures derived from bacterial DNA sequences' *Interdiscip Sci: Comput Life Sci*, 1:81-90.	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Morrison, R. (1993). *Desktop guide to keynotes and confirmatory symptoms.* California: Hahnemann Clinic Publishing.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Morrison, R. (1999). *The Desktop companion*. California: Hahnemann Clinic Publishing.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Morrison, R. (2009). *Carbon: organic and hydrocarbon remedies in homoeopathy.* Kandern: Narayana Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Murphy, R. (1995). *Lotus Materia Medica: Homoeopathic & Spagyric Medicines.* Colorado: Lotus Star Academy Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Murphy, R. (1996). *Homoeopathic Medical Repertory.* Colorado: Lotus Star Academy Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Muscari-Tomaioli, G, Allegri, F. & Miali, E. (2001). Observational study of quality of life in patients with headache, receiving homeopathic treatment. *Homeopathy*, 90: 189-197.	Level III-3	Excluded. Wrong research type or publication type
Naudé DF, Couchman IMS, Maharaj A (2010) Chronic primary insomnia: Efficacy of homeopathic simillimum. *Homeopathy* **99:** 63-68	Level II	Study included within a systematic review in the Overview Report
Novella S (2007) Why Most Published Resesarch Findings are False. Science and Medicine. September.	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type
Oschman, J. (2000). *Energy medicine: the scientific basis.* Edinburgh: Churchill Livingstone.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Oschman, J. (2002). Clinical aspects of biological fields: an introduction for health care professional. Journal of Bodywork and Movement Therapies 6: 2	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Oschman, J. (2003). *Energy medicine in therapeutics and human performance. Oxford: Elsevier.*	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Oschman, J. (2006). Trauma energetics. *Journal of Bodywork and Movement Therapies 10 (1) 21- 34.*	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Oschman, J. (2008). Matrix communication. In: Proceedings of the second metatheory conference, Budapest,	Unable to assign a level of evidence - conference proceedings	Excluded. Wrong research type or publication type
Owen, J.M. Green, B.N. (2004). Homeopathic treatment of headaches: A systematic review of the literature. *Journal of Chiropractic Medicine*, 3: 45-52.	Level I	Systematic review included in Overview Report
Paris, A. Gonnet, N. Chaussard, C. et al (2008). Effect of homeopathy on analgesic intake following knee ligament reconstruction: a phase III monocentre randomized placebo controlled study. *British Journal of Clinical Pharmacology,* 65: 180-187. (Reports results of two trials)	Not applicable. Out of scope	Full text review. Excluded. Out of scope - homeopathy used in conjunction with other therapies where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)

Reference	Level of evidence	Reason for exclusion
Paterson, J. (1943). Report on the mustard gas experiments (Glasgow & London). *British Homoeopathic Journal,* Vo. 33: 1-12.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Pilkington, K, Kirkwood, G, Rampes H, *et al* (2006). Homeopathy for anxiety and anxiety disorders: A systematic review of the research. *Homeopathy*, 95: 151-162.	Level I	Systematic review included in Overview Report
R. Amoroso, I. Diens, C. Varga, (Eds.) Oakland: The Noetic Press.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Rahlfs VW, Mössinger P. (1976). On the treatment of irritable colon. *Arzneimittelforschung*, 26: 2230-2234.	Unable to assign a level of evidence - language	Excluded. Study not published in the English language
Ramachandran, C., Nair, P.K., Clement, R.T., Melnick, S.J. (2007). Investigation of cytokine expression in human leukocyte cultures with two immune-modulatory homoeopathic preparations. J. Altern Complemnt Med.13:403-407.	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Reilly D. (2003). The evidence for homoeopathy. *Glasgow Homoeopathic Hospital DOI: www.adhom.org*	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Reilly, D. & Taylor, M.A. (1985). Potent placebo or potency? A proposed study model with initial findings using homeopathically prepared pollens in hayfever. British Homoeopathic Journal 74: 65-75.	Level II	Study included within a systematic review in the Overview Report
Reilly, D. Taylor, M.A., McSharry, C., Aitchison, T., Carter, R. & Stevenson, R.D. (1994). Is evidence for homoeopathy reproducible? Lancet 344:1601	Level II	Study included within a systematic review in the Overview Report
Reilly, D., Mercer, S. W., Bikker, A. P., Harrison T. (2007). Outcome related to impact on daily living: preliminary validation of the ORIDL instrument. *BMC Health Serv Res*; 7: 139.	Level III-3	Excluded. Wrong research type or publication type
Reilly, D., Taylor, M.A., Beatty, M.G.M., McSharry, C., Aitchison, T. (1986). Is homoeopathy a placebo response? Contolled trial of homoeopathic potency with pollen in hayfever as a model. *British Homoeopathic Journal,* 18: 881-886.	Level II	Study included within a systematic review in the Overview Report
Relton, C., Smith, C., Raw, J. et al (2009). Healthcare provided by a homeopath as an adjunct to usual care for fibromyalgia (FMS): results of a pilot randomised controlled trial. *Homeopathy*, 98: 77-82.	Level II	Study included within a systematic review in the Overview Report
Resch, K.I., Ernst, E. & Garrow, J. A. (2000). Rrandomized controlled study of reviewer bias against unconventional therapy. *J R Soc Med*., 93:164-7.	Level II	Excluded. Wrong outcomes
Rey L (2003)Thermo luminescence of ultra-high dilutions of lithium chloride and sodium chloride. Physica (A) 323: 67-74	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Rey, L. (2003). Thermoluminescence of ultra-high dilutions of lithium chloride and sodium chloride. *Physica A.,* 323:67–74.	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Richardson W R. (2001). Patient benefit survey: Liverpool Regional Department of Homoeopathic Medicine. *Br Homeopath J* ; 90: 158-162.	Level IV	Excluded. Wrong research type or publication type
Riley, D. (1994). Contemporary drug provings. *Journal of the American Institute of Homoeopathy*; 87, 3: 161.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Riley, D. Fischer, M. Singh, B. Haidvogl, M. Hegger, M. (2001). Homoeopathy and conventional medicine: an outcomes study comparing effectiveness in a primary care setting. *J. Altern. Complement. Med.,* 7: 149-159.	Level III-2	Study included within a systematic review in the Overview Report
Ritter, H. (1966). Ein homootherapeutischer doppelter Blindversuch und seine Problematic. *Hippokrates,* Vol. 37, pp 472-476.	Unable to assign a level of evidence - language	Excluded. Study not published in the English language
Rossi E, Crudeli L, Endrizzi C, Garibaldi D (2009) Cost-benefit evaluation of homeopathic versus conventional therapy in respiratory diseases. *Homeopathy* **98:** 2-10	Unable to assign a level of evidence - economic study	Excluded. Wrong research type or publication type
Rostock, M., Naumann, J., Guethlin, C., Guenther, L., Bartsch, H., & Walach, H. (2011). Classical homoeopathy in the treatment of cancer patients – a prospective observational study of two independent cohorts. BMC Cancer, 11:19. www.biomedicalcentral.com/1471-2407/11/19	Not applicable. Out of scope	Full text review. Excluded. Out of scope - homeopathy used in conjunction with other therapies where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)
Rutten A.L., & Stolper, C.F. (2005). The meta-analysis of homoeopathy: the importance of post-publication data. *Homeopathy* 2008; 97: 169-177.	Unable to assign a level of evidence - literature review	Excluded. Wrong research type or publication type
Rutten ALB, Stolper CF (2008) The 2005 meta-analysis of homeopathy: the importance of post-publication data. Homeopathy 97: 169-177	Unable to assign a level of evidence - literature review	Excluded. Wrong research type or publication type
Sackett, D.L., Rosenberg, W.M.C., Muir Gray, J.A., Haynes, R.B., Richardson, W.S. (1996). Evidence based medicine: what it is and what it isen't. *BMJ,* 312:71-72	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Saint-Laudy, J., Belon, P. (1993). Inhibition of human basophil activation by high dilutions of histamine. *Agents Action;* 38:525-527.	Unable to assign a level of evidence - in vitro study	Excluded. Wrong research type or publication type
Samal S, Geckler RE. (2001). Unexpected solute aggregation in water on dilution. *Chem Commun.,* 21:2224–2225.	Unable to assign a level of evidence - laboratory study	Excluded. Wrong research type or publication type
Sankaran, R. & Shah, M. (2010). Survival: *The Reptile*. Mumbai: Homoeopathic Medical Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sankaran, R. (1994a). *The spirit of homoeopathy.* Mumbai: Homeopathic Medical Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sankaran, R. (1994b). *The substance of homoeopathy.* Mumbai: Homoeopathic Medical Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Sankaran, R. (1996). The elements of homoeopathy, Volumes 1 & 2. . Mumbai: Homoeopathic Medical Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sankaran, R. (2000). *The system of homoeopathy.* Mumbai: Homoeopathic Medical Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sankaran, R. (2004a). *An insight into plants, Volume 1.* Mumbai: Homoeopathic Medical Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sankaran, R. (2004b). *An insight into plants, Volume 2.* Mumbai: Homeopathic Medical Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sankaran, R. (2005). *The sensation in homoeopathy.* Mumbai: Homoeopathic Medical Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sankaran, R. (2007). *An insight into plants, Volume 3* Mumbai: Homoeopathic Medical Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sankaran, R. (2008). Experiences with the mineral kingdom. Mumbai: Homoeopathic Medical Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sankaran, R.,& Boldota, S. (2008). Survival: *The Mollusc* Mumbai: Homoeopathic Medical Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Savage, R.H. & Roe, P.F. (1977). A double-blind trial to assess the benefit of Arnica montana in acute stroke illness. *Brit. Hom. J.,* 66:207.	Level III-2	Study included within a systematic review in the Overview Report
Savage, R.H. & Roe, P.F. (1978). A further double-blind trial to assess the benefit of Arnica montana in acute stroke illness. *Brit. Hom. J.* 67:201.	Level III-2	Study included within a systematic review in the Overview Report
Schneider B, Klein P, Weiser M (2005) Treatment of vertigo with a homeopathic complex remedy compared with usual treatments: a meta-analysis of clinical trials. Arzneimittelforschung 55: 23-29	Level III-3	Excluded. Wrong research type or publication type
Schneider, B., Klein, P., Weiser, M. (2005). Treatment of vertigo with a homeopathic complex remedy compared with usual treatments: a meta-analysis of clinical trials. *Arzneimittelforschung*, 55: 23-29.	Level III-3	Excluded. Wrong research type or publication type
Scholten, J. (1993). *Homoeopathy and the Minerals.* Utrecht: Stitchting Alonnissos.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Scholten, J. (1996). *Homoeopathy and the Elements.* Utrecht: Stitchting Alonnissos.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Scholten, J. (2004a). Homoeopathy and science. *Homoeopathic Links: The Journal for Classical Homoeopathy.* Vol.17, No. 3, p.160-164.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Scholten, J. (2004b). Homoeopathy as information science. *Homoeopathic Links: The Journal for Classical Homoeopathy.* Vol.17, No. 4, p. 233-237.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Scholten, J. (2005). *The lanthanides*. Utrecht: Stitchting Alonnissos.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Schroyens, F. (2010). *Synthesis - Repertorium Homoeopathicum Syntheticum.* London: Homoeopathic Book Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Scofield, A.M. (1984). Experimental research in homoeopathy: a critical review. *Brit Hom J*. 73:161.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Sehon, S.R. & Stanley, D.E. (2003). A philosophical analysis of the evidence-based medicine debate BMC Health Services Research 3:14-24.	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type
Sevar, R. (2000). Audit of outcome in 829 consecutive patients treated with homeopathic medicine. *British Homeopathic Journal;* Vol. 89: No.4.	Level III-3	Excluded. Wrong research type or publication type
Shah, J. (2010). *Into the periodic table: the second series*. Kandern: Narayana Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Shang, A. Huwiler-Mutener, K. Nartey, L. Juni, P. Dorig, S., Sterne, J.A. 2005. Are the clinical effects of homeopathy placebo effects? Comparative study of placebo controlled trials of homoeopathy and allopathy. *The Lancet,* Vol. 366, pp. 726-732.	Level I	Systematic review excluded from Overview Report - wrong outcomes
Shang, A. Huwiler-Mutener, K. Nartey, L. Juni, P. Dorig, S., Sterne, J.A. 2005. Are the clinical effects of homeopathy placebo effects? Comparative study of placebo controlled trials of homoeopathy and allopathy. *The Lancet,* Vol. 366, pp. 726-732.	Level I	Systematic review excluded from Overview Report - wrong outcomes
Sharples F, van Haselen R. (1998). Patients' perspectives on using a complementary medicine approach to their health. A survey at the Royal London Homoeopathic Hospital London: NHS Trust.	Level IV	Excluded. Wrong research type or publication type
Shealy CN, Thomlinson RP, Cox RH, Borgmeyer RN. Osteoarthritic pain: a comparison of homeopathy and acetaminophen. AM J Pain Management 1998; 8: 89-91	Level II	Study included within a systematic review in the Overview Report
Sherr, J. (1994). *The dynamics and methodology of homoeopathic provings.* West Malvern: Dynamis Books.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Sherr, J. (1997). *Dynamic provings: Volumes 1 & 2.* USA: Dynamis Books	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Shipley, M. Berry, H. Broster, G. (1983). A controlled trial of homoeopathic treatment of osteoarthritis. *The Lancet,* 8316:97-98.	Level II	Study included within a systematic review in the Overview Report

Reference	Level of evidence	Reason for exclusion
Shore, J., Hogeland, A., & Schriebman, J. (2004). *Birds: Homeopathic remedies from the avian realm*. Kandern: Narayana Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Shuchman M (2007) Commercializing Clinical Trials - Risks and Benefits of the CRO Boom. NEJM Vol. 357:1365-1368. Noo. 14.. October 4 2007	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Sismondo S (2008) Pharmaceutical company funding and its consequences: A qualitative systematic review. Contemporary Clinical Trials 29: 109-113	Level I	Systematic review excluded from Overview Report - wrong intervention
Smallwood, C. (2005) Homeopathy. In: The role of complementary and alternative medicine in the NHS. FreshMinds UK. Pg 47-56	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Smit, E. Pertorius, E. Anderson, R. Oomenn, J. Potjo, M. (2008). Differentiation of human monocytes in vitro following exposure to Canova in the absence of cytokines. *Ultrastruct Pathol.,* 32:147-152.	Unable to assign a level of evidence - in vitro study	Excluded. Wrong research type or publication type
Smith CA. Homoeopathy for induction of labour. Cochrane Database of Systematic Reviews 2003, Issue 4. Art. No.: CD003399. DOI: 10.1002/14651858.CD003399	Level I	Systematic review included in Overview Report
Smith, C.A. (2004). Homoeopathy for induction of labour *(Cochrane Review).* In: The Cochrane Library. Chichester, UK: John Wiley & Sons, Ltd. CD003399.	Level I	Systematic review included in Overview Report
Spence D, Thompson E, Barron S (2005) Homeopathic treatment for chronic disease: A 6-year university hospital based outpatient observational study. Journal of Alternative and Complementary Medicine 5: 793-798	Level III-3	Excluded. Wrong research type or publication type
Spence, D. et al (2005). Homoeopathic treatment for chronic disease: a 6 year, University Hospital Outpatient Observational Study. *J Alt Comp Med.,* 11:793-798	Level III-3	Excluded. Wrong research type or publication type
Steen R G (2010) Retractions in the scientific literature: do authors deliberately commit scientific fraud? J Med Ethics. DOI: 10.1136/jme.2010.038125. http://jmebmh.com	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type
Steinsbekk, A. (2005). Patients' assessments of the effectiveness of homeopathic care in Norway: A prospective observational multi-centre outcome study. *Homeopathy,* Volume 94: 1.	Level III-3	Excluded. Wrong research type or publication type
Stevinson, C. Devaraj, V.S. Fountain-Barber A. *et al* (2003). Homeopathic arnica for prevention of pain and bruising: randomized placebo-controlled trial in hand surgery. *Journal of the Royal Society of Medicine*, 96: 60-65.	Level II	Study included within a systematic review in the Overview Report
Straumsheim, P.A. Borchgrevink, C.F., Mowinkel, P. Kierulf, H. & Hafslund, O. (1997). Homoeopathic treatment of migraine: a double-blind, placebo-controlled study of 68 patients. *Dynamis,* 2:18-22.	Level II	Study included within a systematic review in the Overview Report
Swayne J. (1992). The cost, effectiveness of homoeopathy.A pilot study, proposals for future research*. Br Homoeopath J;* 81: 148–150.	Unable to assign a level of evidence - economic study	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Tabarrok A (2005) Why Most Published Research Findings are False. Economics / Permalink. September	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type
Taylor MA, Reilly D, Llewellyn-Jones RH et al (2000) Randomised controlled trials of homoeopathy versus placebo in perennial allergic rhinitis with overview of four trial series. British Medical Journal 371: 471-476	Level II	Study included within a systematic review in the Overview Report
Taylor, J & Jacobs, J. Homeopathic ear drops as an adjunct to standard therapy in children with acute otitis media. Homeopathy(2011)100, 109-15	Not applicable. Out of scope	Full text review. Excluded. Out of scope - homeopathy used in conjunction with other therapies where the design of the study confounds the results (i.e. where the specific effect of homeopathy cannot be determined)
Taylor, M.A., Reilly, D., Llewellyn-Jones, R.H., McSharry, C., Aitchison, T.C. (2000). Randomized controlled trial of homeopathic versus placebo in perennial allergic rhinitis with overview of four trial series. *British Medical Journal* 321: 471-476.	Level II	Study included within a systematic review in the Overview Report
The Lancet (2005). Editorial. The end of homeopathy *The Lancet;* 366:690.	Unable to assign a level of evidence - editorial	Excluded. Wrong research type or publication type
The Lancet (2005). Editorial. The end of homeopathy *The Lancet;* 366:690.	Unable to assign a level of evidence - editorial	Excluded. Wrong research type or publication type
Thompson, E. (2004). A preliminary audit investigating remedy reactions including adverse events in routine homeopathic practice. *Homeopathy,* 93;203-209	Level III-3	Excluded. Wrong research type or publication type
Thompson, E. A., Mathie, R T, Baitson, E S, Barron, S J, Berkovitz, S R, Brands, M, Fisher, P, Kirby, T M, Leckridge, R W, Mercer, S W, Nielsen H J, Ratsey, D H K, Reilly, D, Roniger, H, Whitmarsh, T.E. (2008). Towards standard setting for patient-reported outcomes in the NHS homeopathic hospitals. *Homeopathy*, 97:114-121.	Unable to assign a level of evidence - pilot data collection study	Excluded. Wrong research type or publication type
Tiexiera, M.Z. (2006). Evidence of the principle of similitude in modern fatal iatrogenic events. *Homoeopathy;* 95:229-236.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Tiexiera, M.Z. (2007). Bronchodilators, fatal asthma, rebound effect and similitude. *Homoeopathy;* 96:135-137.	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type
Tobin L. (2010) GlaxoSmithKline in £1.6bn payout over drug legal threat. London evening Standard. 15.7.2010	Unable to assign a level of evidence - news article	Excluded. Wrong research type or publication type
Towheed, T. & Anastassiades, T. (2000). Glucosamine and chondroitin for treating the symptoms of osteoarthritis: evidence is widely touted, but incomplete. *Journal of the American Medical Association,* Vo. 283, pp. 1469-75.	Unable to assign a level of evidence - editorial	Excluded. Wrong intervention

Reference	Level of evidence	Reason for exclusion
Trichard M, Chaufferin G, Nicoloyannis N. Pharmacoeconomic comparison between homeopathic and antibiotic treatment strategies in recurrent acute rhinopharyngitis in children. Homeopathy 2005l 94: 3-9	Unable to assign a level of evidence - economic study	Full text review. Excluded. Wrong research type or publication type
Tuminello, P. (1997). *Rhus Glabra* St. Leonards: The Medicine Way	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Tuminello, P. (2005). *Twelve Jewels* St. Leonards: The Medicine Way	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
U.K. Government response to the Science and Technology Committee report: 'Evidence Check 2: Homoeopathy,' 2010, presented to Parliament by the Secretary of State for Health by Command of Her Majesty, available at <http://www.dh.gov.uk/prod	Unable to assign a level of evidence - government report	Excluded. Wrong research type or publication type
Ullman D. (2003). Controlled clinical trials evaluating the homeopathic treatment of people with human immunodeficiency virus or acquired immune deficiency syndrome. *Journal of Alternative and Complementary Medicine*, 9: 133-141.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
US Department of Justice - Civil Division (2010) Fraud Statistics - Health and Human Services	Unable to assign a level of evidence - department of justice report	Excluded. Wrong research type or publication type
Ustianowski, P. (1974) A clinical trial of staphysagria in post-coital cystitis. *British Homoeopathic Journal*, Vol. 63, pp. 276-277.	Level III-3	Full text review. Excluded. Wrong research type or publication type
Vallance, A. (1998). Can biological activity be maintained at ultra-high dilution? An over-view of homoeopathy, evidence and Bayesian philosophy. *J. Altern & Complem. Med.,* 4: 1-49.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
van Haselen RA, Fisher PAG (2000) A randomized controlled trial comparing topical piroxicam gel with a homeopathic gel in osteoarthritis of the knee. Rheumatology 39: 714-719	Level II	Study included within a systematic review in the Overview Report
Van Wassenhoven M (2008) Scientific framework of homeopathy: Evidence-based homeopathy. *International Journal of High Dilution Research* **7:**28-50	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Van Wassenhoven M (2010) Scientific framework of homeopathy: Evidence-based homeopathy 2010.After 65th LMHI Congress	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Van Wassenhoven M (2012) Scientific framework of homeopathy: Evidence-based homeopathy 2012.After 66th LMHI Congress	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Vermeulen, F. (1992). *Synoptic Materia Medica 1.* The Netherlands: Emryss Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Vermeulen, F. (1994). *Concordant Materia Medica* The Netherlands: Emryss Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Vermeulen, F**. (**1996). *Synoptic Materia Medica 2*. The Netherlands: Emryss Publishers	Unable to assign a level of	Excluded. Wrong research type or

Reference	Level of evidence	Reason for exclusion
	evidence - book	publication type
Vermeulen, F. (2000). *Fungi – kingdom fungi.* Spectrum Materia Medica Volume 2, The Netherlands: Emryss Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Vermeulen, F. (2005). *Monera - kingdom bacteria and viruses.* Spectrum Materia Medica Volume 1. The Netherlands: Emryss Publishers	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Vickers A, Smith C. Homoeopathic Oscillococcinum for preventing and treating influenza and influenza-like syndromes. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD001957. DOI: 10.1002/14651858.CD001957.pub4.	Level I	Systematic review excluded from Overview Report - superseded publication
Vickers A, Smith C. Homoeopathic Oscillococcinum for preventing and treating influenza and influenza-like syndromes. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD001957. DOI: 10.1002/14651858.CD001957.pub4.	Level I	Systematic review included in Overview Report
Vickers, A. & Smith, C. 2006 Homoeopathic oscillococcinum for preventing and treating influenza and influenza-like syndromes. *Cochrane Database of Systematic Reviews:* Issue 3, Art No. CD001957, pp. 2-31.	Level I	Systematic review excluded from Overview Report - superseded publication
Vithoulkas, G. (2010) *Materia Medica Viva 1 – 12* Kandern: Narayana Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Vonsyhomeopathy.wordpress.com/2010/02/27/stop-funding-nhs-homeopathy-mps-urgwho-are-these-mps/#more-293	Unable to assign a level of evidence - website	Excluded. Wrong research type or publication type
Wagner, E. et. Al. 2009. Science editors' views on publication ethics: Results of an International Survey. Journal of Medical Ethics. 35 (6): 348-353.	Level IV	Excluded. Wrong research type or publication type
Walach H (2001) The efficacy paradox in randomized controlled trials of CAM and elsewhere: Beware of the placebo trap. The Journal of Alternative and Complementary Medicine 7: 213-218	Unable to assign a level of evidence - editorial	Excluded. Wrong research type or publication type
Walach H. (2006). 'Circular instead of hierarchical: methodological principles for the evaluation of complex interventions,' BMC Medical Research Methodology, Vol. 6, no. 29, accessed online on 2nd February 2006, DOI: http://www.biomedcentral.com/1471-2288/6/29.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Walach, H, Jonas WB, Lewith GT (2002). The role of outcomes research in evaluating complementary and alternative medicine. *Alternative Therapies in Health and Medicine*, 8: 88-95.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type
Walach, H. & Jonas, B. (2002). Homoeopathy. In G. Lewith, G., B. Jonas & H. Walach. Clinical research in complementary therapies, pp. 229-246. London: Harcourt Publishers.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Walach, H. (1993). Does a highly diluted homoeopathic drug act as a placebo in healthy volunteers? Experimental study of Belladonna 30C in double-blind cross-over design: a pilot study. *J. Psychosomatic Res.,* 37:851	Level II	Full text review. Excluded. Wrong outcomes

Reference	Level of evidence	Reason for exclusion
Walach, H. (1998). Methodology beyond controlled clinical trials. In: E. Ernst, E.G. Hahn, (Eds.) Homoeopathy: a critical appraisal, pp. 48-59. London: Butterworth Heinemann.	Unable to assign a level of evidence - book	Excluded. Wrong research type or publication type
Walach, H. Gaus, W. Haeusler, W. et al (1997). Classical homoeopathic treatment of chronic headaches: a double-blind, randomised, placebo-controlled study. *Cephalalgia* 17:119-126.	Level II	Study included within a systematic review in the Overview Report
Weatherley-Jones E, Nicholl JP, Thomas KJ, et al. A randomized, controlled, triple-blind trial of the efficacy of homeopathic treatment for chronic fatigue syndrome. J Psychosom Res 2004; 56: 189-97	Level II	Study included within a systematic review in the Overview Report
Website: http://knol.google.com/k/scientific-research-in-homeopathy#	Unable to assign a level of evidence - website not found	Excluded. Wrong research type or publication type
Website: http://www.britishhomeopathic.org/export/sites/bha_site/research/evidence_by_condition_refs.pdf	Unable to assign a level of evidence - list of clinical trials	Excluded. Wrong research type or publication type
Website: http://www.facultyofhomeopathy.org/research/	Unable to assign a level of evidence - overview of evidence base	Excluded. Wrong research type or publication type
Website: http://www.homeopathyoz.org/downloads/LIGA-EvidenceBaseForHomeopathy.pdf	Unable to assign a level of evidence - website not found	Excluded. Wrong research type or publication type
Website: www.ismp.org/QuarterWatch/2009Q4.pdf	Unable to assign a level of evidence - FDA monitoring report	Excluded. Wrong research type or publication type
Weigart, F.A.C., Souren, J.E.M., Van Wijk, R. (1999). Stimulation of survival apacity in heat-shocked cells by subsequent exposure to minute amounts of chemical stressors: the role of similarity in hsp-inducing effects. *Hum Exp Toxicol;* 18:460-470.	Unable to assign a level of evidence - in vitro study	Excluded. Wrong research type or publication type
Weiser, M. & Clasen, B. (1994). Randomized, placebo-controlled, double-blind study of the clinical efficacy of the homeopathic Euphorbium compositum-S nasal spray in cases of chronic sinusitis. *Forschende Komplementärmedizin*, **1**: 251-259. *(Reports results of two trials)*	Level II	Study included within a systematic review in the Overview Report
Wells, S.U. Suanjak-Traidl, E., Weber, S., Scherer_Pongratz, W. Frass, M. Endler, P.C. Spranger, H. Lothaller, H. (2007). Pre-treatment with thyroxine (10e8) and the effect of homoeopathically prepared thryoxine (10-30) on highland frogs-a multi-researcher study. *Res Compl Med/Forsch Komplementared*, 14:353-357.	Unable to assign a level of evidence - animal study	Excluded - Non-human study
Whitmarsh,T.E., Coleston_Shields, D.M., Steiner, T.J. (1997). Double-blind, randomised, placebo-controlled study of homoeopathic prophylaxis of migraine. *Cephalalgia* 17:600-604.	Level II	Study included within a systematic review in the Overview Report

Reference	Level of evidence	Reason for exclusion
Wiesenauer M, Lüdtke R (1996). A meta-analysis of the homeopathic treatment of pollinosis with Galphimia glauca. *Forschende Komplementärmedizin und Klassische Naturheilkunde*, 3: 230-236.	Unable to assign a level of evidence - language	Excluded. Study not published in the English language
Wilson, A., & Henry, D. (1992). Meta-analysis (Part 2): Assessing the quality of published meta-analyses. *Medical Journal of Australia,* Vol. 156, pp. 173-187.	Unable to assign a level of evidence - commentary	Excluded. Wrong research type or publication type
Witt C, Keil T, Selim D et al (2005) Outcome and costs of homeopathic and conventional treatment strategies: A comparative cohort study in patients with chronic disorders. Complementary Therapies in Medicine 13: 79-86	Level III-2	Study included within a systematic review in the Overview Report
Witt C, Keil T, Selim D, Roll S, Vance W, Wegscheider K, Willlich SN (2005) Outcome and costs of homoeopathic and conventional treatment strategies: A comparative cohort study in patients with chronic disorders. *Complementary Therapies in Medicine* **13:** 79-86	Level III-2	Study included within a systematic review in the Overview Report
Witt CM, Bluth M, Albrecht H et al (2007) The in vitro evidence for an effect of high homeopathic potencies - A systematic review of the literature. Complementary Therapies in Medicine 15: 128-138	Level I	Systematic review excluded from Overview Report - wrong outcomes
Witt CM, Bluth M, Albrecht H, Weiβhuhn TER, Baumgartner S, Willich SN (2007) The in vitro evidence for an effect of high homeopathic potencies - A systematic review of the literature. *Complementary Therapies in Medicine* **15:** 128-138	Level I	Systematic review excluded from Overview Report - wrong outcomes
Witt CM, Lüdtke R, Baur R, Willich SN (2005b) Homeopathic medical practice: Long-term results of a cohort study with 3,981 patients. BMC Public Health 5: 115	Level III-3	Excluded. Wrong research type or publication type
Witt, C.M. Bluth, M. Albrecht, H. Weibhuhn, T. Baumgartner, S. Willich, S.N. (2007). The in-vitro evidence for the effect of high homoeopathic potencies – a systematic review of the literature. *Compl Therp Med* 15:128-138.	Level I	Systematic review excluded from Overview Report - wrong outcomes
Witt, J. (2005). Outcome and costs of homoeopathic and conventional treatment strategies: a comparative cohort study in patients with chronic disorders. Comp. Ther. Med. 13: 79-86.	Level III-2	Study included within a systematic review in the Overview Report
Wolf, M. Tamaschke, C. Mayer, W. Heger, M. (2003). Efficacy of Arnica in varicose vein surgery: results of a randomized, double-blind, placebo-controlled pilot study. *Forschende Komplementärmedizin und Klassische Naturheilkunde*, 10: 242-247.	Level II	Full text review. Excluded. Study not published in the English language
Xue, C., Zhang, C., Lin, V., Da Costa C. & Story, D.F. (2007). Complementary Medicine use in Australia: a national population-based survey. The Journal of Alternative and Complementary Medicine, 13(6): 643-650	Level IV	Excluded. Wrong research type or publication type
Xue, C.C., Zhang L., Lin V., & Story D.F. (2006). The Use of Complementary and Alternative Medicine in Australia. *Health Issues*, 88:12-5.	Unable to assign a level of evidence - narrative review	Excluded. Wrong research type or publication type

Reference	Level of evidence	Reason for exclusion
Xue, C.C., Zhang, A.L., Lin, V., Myers, R., Polus, B., Story D.F. (2008). Acupuncture, chiropractic and osteopathy use in Australia: a national population survey. *BMC Public Health*; 8:105.	Level IV	Excluded. Wrong research type or publication type
Yakir M, Kreitler S, Brzezinski A, et al (2001) Effects of homeopathic treatment in women with premenstrual syndrome: A pilot study. Brithis Homeopathy Journal 90: 148-153	Level II	Study included within a systematic review in the Overview Report
Zabolotnyi, D.I., Kneis, K.C., Richardson, A., et al (2007). Efficacy of a complex homeopathic medication (Sinfrontal) in patients with acute maxillary sinusitis: a prospective, randomized, double-blind, placebo-controlled, multicenter clinical trial. *Explore (NY)*, 3: 98-109.	Level II	Study included within a systematic review in the Overview Report
Zell J, Connert WD, Mau J, Feuerstake G. Treatment of acute sprains of the ankle. Controlled double-blind trial to test the effectiveness of a homeopathic ointment. Fortschr Med 1988; 106: 96-100	Level II	Study included within a systematic review in the Overview Report
Zeng, H., Wilson, L.D., Walker, V.K., Ripmeester, J.A. (2006). Effect of anti-freeze proteins on the nucleation, growth, and the memory effect during tetrahydrofuran clathrate hydrate formation. *J Am Chem Soc.,* 128:2844-2850.	Unable to assign a level of evidence - not an intervention study	Excluded. Wrong research type or publication type
Zhang, A.L., Xue, C.C., Lin, V. & Story DF. (2007). Complementary and alternative medicine use by older Australians. *Ann N Y Acad Sci*., 14:204-15.	Level IV	Excluded. Wrong research type or publication type

Appendix B List of included studies

Adler UC, Paiva NMP, Cesar AT, Adler MS, Molina A, Padula AE, Calil HM (2009). Homeopathic individualized Q-potencies versus fluoxetine for moderate to severe depression: double-blind, randomized non-inferiority trial. eCAM doi: 10.1093/ecam/nep114.

Frass M, Dielacher C, Linkesch M, Endler C, Muchitsch I, Schuster E, Kaye A (2005). Influence of potassium dichromate on tracheal secretions in critically ill patients. CHEST 127: 936-941.

Hart O, Mullee MA, Lewith G, Miller J (1997). Double-blind, placebo-controlled, randomized clinical trial of homoeopathic arnica C30 for pain and infection after total abdominal hysterectomy. Journal of the Royal Society of Medicine 90: 73-78.

Karow JH, Abt HP, Fröhling M, Ackermann H (2008). Efficacy of Arnica montana D4 for healing of wounds after Halluz valgus surgery compared to diclofenac. Journal of Alternative and Complementary Medicine 14: 17-25.

Seeley BM, Denton AB, Ahn MS Maas CS (2006). Effect of homeopathic Arnica montana on bruising in face-lifts. Archives of Facial Plastic Surgeons 8: 54-59.

Sinha MN, Siddiqui VA, Nayak C, Singh V, Dixit R, Dewan D, Mishra A (2012). Randomised controlled pilot study to compare Homeopathy and conventional therapy in Acute Otitis Media. Homeopathy 101: 5-12.

Tveiten D, Bruset S, Borchgrevink CF, Norseth J (1998). Effects of the homoeopathic remedy Arnica D30 on marathon runners: a randomised, double-blind study during the 1995 Oslo marathon. Complementary Therapies in Medicine 6: 71-74.

Vickers A, Fisher P, Smith C, Wyllie SE, Lewith GT (1998). Arnica 30X is ineffective for muscle soreness after long-distance running: a randomised, double-blind, placebo controlled trial. Clinical Journal of Pain 14: 227-231.

Waldschütz R, Klein P (2008). The homeopathic preparation Neurexan vs. valerian for the treatment of insomnia: an observational study. Scientific World Journal 8: 411-420.

Appendix C Data extraction and quality assessment forms

The quality assessment form for each study is presented immediately after its data extraction form.

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference: Adler UC, Paiva NMP, Cesar AT, Adler MS, Molina A, Padula AE, Calil HM (2009). Homeopathic individualized Q-potencies versus fluoxetine for moderate to severe depression: double-blind, randomized non-inferiority trial. eCAM doi: 10.1093/ecam/nep114.</td></tr>
<tr><td colspan="5">Affiliation/source of funds: Not reported
Conflicts of interest: Not reported</td></tr>
<tr><td colspan="2">Study design:
Randomised, double-blind, double-dummy trial</td><td>Level of evidence:
Level II</td><td colspan="2">Location/setting:
Outpatient clinic, Sao Paulo, Brazil</td></tr>
<tr><td colspan="2">Intervention:
Individualised homeopathy. Various Q-potencies, one drop, 3 times a week in the morning; and matching placebo.
Concomitant psychoactive medications: 1 patient using clonazepam, 1 patient using diazepam
Sample size: n=48</td><td colspan="3">Comparator(s):
20 mg fluoxetine-hydrochloride, once daily; and matching placebo
Concomitant psychoactive medications: 3 patients taking clonazepam, 2 patients taking diazepam
Sample size: n=43</td></tr>
<tr><td colspan="5">Inclusion criteria: Patients referred to the outpatient clinic of Homeopathy and Depression of Jundiai Medical School (Sao Paulo, Brazil) who met DSM-IV criteria for depression (single or recurrent episode) following a Structured Clinical Interview
Exclusion criteria: Psychosis, mania, hypomania or any other Axis I disorder except panic disorder, personality disorders, history of seizures, history of alcohol or drug abuse 1 year prior to the screening, antidepressant use up to 30 days before screening, pregnancy or lactation, age <18 years, MADRS score <15, recent suicide planning or attempts</td></tr>
<tr><td colspan="5">Population characteristics
Patients with moderate to severe depression
Intervention and comparator group: Mean age 41.9±12.3
Comparator group: Mean age 44.3±11.8
Total study size: N=91</td></tr>
<tr><td colspan="5">Length of follow-up: 8 weeks</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation:
Adequate concealment of allocation</td><td>Comparison of study groups:
Homeopathy vs active comparator. No significant differences in baseline characteristics between groups. It was not reported if the differences in concomitant psychoactive medications between treatment groups were significant or not</td><td>Blinding:
Double-blind</td><td>Treatment/ measurement bias:
Low risk of bias</td><td>Follow-up (ITT):
55 of the 91 randomised participants completed the trial</td></tr>
<tr><td colspan="5">SIGN quality assessment (descriptive): Evidence level 1+. Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions.</td></tr>
<tr><td colspan="5">RESULTS

Overall conclusions: “This study indicates the non-inferiority of individualised homeopathic Q-potencies as compared to fluoxetine in acute treatment of outpatients with moderate to severe depression.”</td></tr>
<tr><td>Trial (N)
Quality</td><td>Intervention</td><td>Comparator</td><td>Outcome</td><td>Results</td></tr>
<tr><td>Adler et al (2009) [Level II]
SIGN EL</td><td>Individualised homeopathy. Various Q-potencies, one drop, 3 times a week in the</td><td>20 mg fluoxetine-hydrochloride, once daily; and matching placebo</td><td>MADRS scores</td><td>No significant difference. Individualised homeopathic Q-potencies were not inferior to fluoxetine</td></tr>
</table>

1++ N=91	morning; and matching placebo. Concomitant psychoactive medications: 1 patient using clonazepam, 1 patient using diazepam	Concomitant psychoactive medications: 3 patients taking clonazepam, 2 patients taking diazepam	Response rate	No significant difference
			Remission rate	No significant difference
			Tolerability (side effects rate)	No significant difference

Abbreviations: EL, evidence level; ITT, intention to treat; MADRS, Montgomery and Asberg Depression Rating Scale; Q-potencies, Quinquagintamillesmial; SIGN, Scottish Intercollegiate Guidelines Network.

SIGN	4 Methodology Checklist 2: Controlled Trials

Study identification (*Include author, title, year of publication, journal title, pages*)

Adler UC, Paiva NMP, Cesar AT, Adler MS, Molina A, Padula AE, Calil HM (2009). Homeopathic individualized Q-potencies versus fluoxetine for moderate to severe depression: double-blind, randomized non-inferiority trial. eCAM doi: 10.1093/ecam/nep114.

Guideline topic: Effectiveness of homeopathy for a specific clinical condition	Key Question No: 1

Checklist completed by: OPTUM

SECTION 1: INTERNAL VALIDITY

In a well conducted RCT study…		***5 In this study this criterion is:***
1.1	The study addresses an appropriate and clearly focused question.	Well covered
1.2	The assignment of subjects to treatment groups is randomised	Well covered
1.3	An adequate concealment method is used	Well covered
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Well covered
1.5	The treatment and control groups are similar at the start of the trial	Well covered
1.6	The only difference between groups is the treatment under investigation	Well covered
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Well covered
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	Homeopathy group: 19/48 (40%) Comparator group: 17/43 (40%)
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias? *Code ++, +, or –*	1+ (downgraded from 1++ due to high loss to follow up)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	No, the results of 2 patients in the homeopathy group and 5 patients in the comparator group were confounded by concomitant psychoactive medications. It is also noted by the authors that the use of individualised homeopathy is a "severe obstacle for any double-blind trial"
2.3	Are the results of this study directly applicable to the	Yes

	patient group targeted by this guideline?	
2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.	
	This study found no significant difference between homeopathy and an active comparator for any of the outcomes measured. The authors concluded that the study "indicates the non-inferiority of individualised homeopathic Q-potencies as compared to fluoxetine in acute treatment of outpatients with moderate to severe depression".	

STUDY DETAILS

Reference: Frass M, Dielacher C, Linkesch M, Endler C, Muchitsch I, Schuster E, Kaye A (2005). Influence of potassium dichromate on tracheal secretions in critically ill patients. CHEST 127: 936-941.

Affiliation/source of funds: Ludwig Boltzmann Institute for Homeopathy, Vienna, Austria; University of Vienna, Vienna, Austria; Texas Tech University, Texas, USA
Conflicts of interest: not reported

Study design:	**Level of evidence:**	**Location/setting:**
Randomised, double-blind, placebo-controlled trial	Level II	Karlsruhe, Germany

Intervention:	**Comparator(s):**
Potassium dichromate C30, 5 globules administered twice daily at intervals of 12 hours **Sample size:** n=25	Placebo **Sample size:** n=25

Inclusion criteria: Documented history of tobacco use and COPD for at least 10 years before acute deterioration; spontaneous breathing with CPAP with a FIO_2 varying between 0.21 and 0.3, and possible airway pressure from 5 to 7cm H_2O after weaning from controlled mechanical ventilation. Additionally, extubation was impossible due to profuse tenacious stringy, tracheal secretions according to the criteria listed above
Exclusion criteria: Signs of additional lung diseases other than COPD at the time of enrolment or during the study observational period; positive blood culture results during the period of controlled mechanical ventilation; concomitant disease of the larynx and trachea obstructing the airway or inhibiting the extubation process; concomitant heart disease; need for catecholamines; pregnancy

***Population characteristics*:** critically ill patients with a history of tobacco use and COPD
Intervention group: mean age 69.2±9.1 years; 19 male, 6 female; n=25
Comparator group: mean age 68.4±10.1 years; 20 male, 5 female; n=25
Total study size: N=55 randomised, n=50 evaluated

Length of follow-up: 18 months

INTERNAL VALIDITY

Allocation: Adequate concealment. An independent physician not involved in the study held the computer-generated code for randomisation.	Comparison of study groups: Homeopathy vs placebo. No statistically significant differences in baseline characteristics/demographics between the two groups	Blinding: Double-blind for both patients and assessors	Treatment/ measurement bias: High risk of bias. It is poorly addressed if patients remained on other medications during the trial period. The trial also lasted 18 months but only results of days 1 and 2 of treatment are presented.	Follow-up (ITT): 5 patients were excluded after randomisation. N=50 patients were evaluated (n=25 in both groups)

SIGN quality assessment (descriptive): Evidence level 1-. Most of the SIGN criteria have been fulfilled, however it is poorly addressed if the treatment under investigation was the only difference between the groups. This is a critical confounding factor that may invalidate the results. In addition, the trial lasted 18 months but only the results of days 1 and 2 of treatment are presented for tracheal secretions (the primary outcome of the study). There is thus a high risk of bias in this study.

RESULTS

Conclusions: "These data suggest that potentized (diluted and vigorously shaken) potassium dichromate may help to decrease the amount of stringy tracheal secretions in COPD patients".

Trial (N) *Quality*	Intervention	Comparator	Outcome	Results
Frass et al (2005) [Level II] *SIGN EL 1-* N=55	Potassium dichromate C30, 5 globules administered twice daily at intervals of 12 hours	Placebo	Tracheal secretions on day 1	No significant difference
			Tracheal secretions on day 2	Significantly reduced in favour of homeopathy (P<0.0001) • Homeopathy: 1.52±0.59 mL • Placebo: 2.44±0.65 mL

			Extubation	Could be performed significantly earlier in homeopathy group (P<0.0001) • Homeopathy: 2.88±1.20 days • Placebo: 6.12±3.13 days
			Length of stay in intensive care unit	Significant difference in favour of homeopathy (P<0.0001) • Homeopathy: 4.20±1.61 days • Placebo: 7.68±3.60 days

Abbreviations: COPD, chronic obstructive pulmonary disease; CPAP, continuous positive airway pressure; EL, evidence level; FIO_2, Fraction of inspired oxygen; ITT, intention to treat; SIGN, Scottish Intercollegiate Guidelines Network.

SIGN	**6 Methodology Checklist 2: Controlled Trials**

Study identification (*Include author, title, year of publication, journal title, pages*)

Frass M, Dielacher C, Linkesch M, Endler C, Muchitsch I, Schuster E, Kaye A (2005). Influence of potassium dichromate on tracheal secretions in critically ill patients. CHEST 127: 936-941.

Guideline topic: Effectiveness of homeopathy for a specific clinical condition	Key Question No: 1

Checklist completed by: OPTUM

SECTION 1: INTERNAL VALIDITY

In a well conducted RCT study…		***7 In this study this criterion is:***
1.1	The study addresses an appropriate and clearly focused question.	Well covered
1.2	The assignment of subjects to treatment groups is randomised	Well covered
1.3	An adequate concealment method is used	Well covered
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Well covered
1.5	The treatment and control groups are similar at the start of the trial	Well covered
1.6	The only difference between groups is the treatment under investigation	Poorly addressed
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Well covered
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	Homeopathy group: 2/27 patients (7%) Placebo group: 3/28 patients (11%)
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias? *Code ++, +, or –*	1-
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	The key limitation in this study is that it is unclear if homeopathy was the only intervention that was used, or if the patients remained on other medications in both study groups that may have helped to relieve tracheal secretions.
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes

2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.
	The authors concluded that "the data suggest that potentized (diluted and vigorously shaken) potassium dichromate may help to decrease the amount of stringy tracheal secretions in chronic obstructive pulmonary disease patients". The evidence reviewer notes that this conclusion is consistent with the data presented in the study. However, a crucial limitation that was not addressed was whether the patients remained on other medications during the trial period, which may have affected tracheal secretions. In addition, given that the study lasted 18 months, the evidence reviewer is cautious that only results of tracheal secretions (the primary outcome) at days 1 and 2 of treatment are presented. There is thus a high risk of bias in this study.

STUDY DETAILS

Reference: Hart O, Mullee MA, Lewith G, Miller J (1997). Double-blind, placebo-controlled, randomized clinical trial of homoeopathic arnica C30 for pain and infection after total abdominal hysterectomy. Journal of the Royal Society of Medicine 90: 73-78.

Affiliation/source of funds: NR
Conflicts of interest: NR

Study design:	**Level of evidence:**	**Location/setting:**
Randomised, double-blind, placebo-controlled trial	Level II	Princess Anne Hospital, Southamptom

Intervention: Two doses of Arnica C30 taken in the 24 h postoperatively, and then three doses each day for 5 days postoperatively starting on the morning after the operation **Sample size:** n=38	**Comparator(s):** Placebo **Sample size:** n=35

Inclusion criteria: Women booked for total abdominal hysterectomies at the Princess Anne Hospital, Southampton, between January and March 1995
Exclusion criteria: NR

Population characteristics
Intervention group: Median age (range): 40 years (25-53)
Comparator group: Median age (range): 43 years (32-76)
Total study size: N=93

Length of follow-up: 2 weeks

INTERNAL VALIDITY

Allocation: Appropriate method of randomisation. Allocation concealment not reported	Comparison of study groups: Placebo patients had a higher mediation age. Length of operation was longer in those patients receiving Arnica. Other baseline characteristics were comparable between groups	Blinding: Double-blind	Treatment/ measurement bias: Low risk of bias. Each outcome is clearly defined	Follow-up (ITT): 20 women did not complete protocol treatment (9 from *Arnica* group and 11 from placebo). Of these, 9 were excluded because they failed to comply, 9 had their operations cancelled or changed within 24 h and 2 withdrew

SIGN quality assessment (descriptive): Evidence level 1-. "Few or no criteria fulfilled. The conclusions of the study are thought likely or very likely to alter"
Notes: patients were permitted to remain on analgesics, non-steroidal anti-inflammatories and opioids during the course of treatment

RESULTS

Overall conclusions: "We conclude that arnica in homoeopathic potency had no effect on postoperative recovery in the context of our study"				
Trial (N)	Intervention	Comparator	Outcome	Results
Hart et al (1997) [Level II] *SIGN EL 1-* N=93	Two doses of Arnica C30 taken in the 24 h postoperatively, and then three doses each day for 5 days postoperatively starting on the morning after the operation	Placebo	Infection rate (need for the prescription of systemic antibiotics)	No significant difference
			Median time spent in hospital	No significant difference
			Pain at 2-week follow up	No significant difference
			Analgesic intake	No significant difference
			Mean pain score over 5 days as measured by VAS	No significant difference

Abbreviations: ITT, intention to treat; NR, not reported; SIGN, Scottish Intercollegiate Guidelines Network; VAS, Visual Analogue Scale.

SIGN

7.1.1 Methodology Checklist 2: Controlled Trials

Study identification (*Include author, title, year of publication, journal title, pages*)

Hart O, Mullee MA, Lewith G, Miller J (1997). Double-blind, placebo-controlled, randomized clinical trial of homoeopathic arnica C30 for pain and infection after total abdominal hysterectomy. Journal of the Royal Society of Medicine 90: 73-78.

Guideline topic: Effectiveness of homeopathy for a specific clinical condition	Key Question No: 1

Checklist completed by: OPTUM

Section 1: Internal validity

	In a well conducted RCT study…	7.1.1.1 **In this study this criterion is:**
1.1	The study addresses an appropriate and clearly focused question.	Well covered
1.2	The assignment of subjects to treatment groups is randomised	Adequately addressed
1.3	An adequate concealment method is used	Not addressed
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Well covered
1.5	The treatment and control groups are similar at the start of the trial	Adequately addressed
1.6	The only difference between groups is the treatment under investigation	Adequately addressed
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Well covered
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	Homeopathy group: 9/47 (19%) Comparator group: 11/46 (24%)
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias? Code ++, +, or –	1- (downgraded from ++ due to allocation concealment not described, high loss to follow up and the likely confounding influence of analgesics)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall	No, patients were permitted to remain on analgesics, non-steroidal anti-inflammatories and opioids during the course of treatment

	effect is due to the study intervention?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes
2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.	
	The authors concluded that ""…arnica in homoeopathic potency had no effect on postoperative recovery in the context of our study". The results for all of the outcomes examined support this conclusion, however, this study was subject to a high risk of bias. These include selection bias issues arising from lack of allocation concealment and high loss of follow up. In addition, only 12 arnica and 10 placebo patients completed the 10^{th} and final pain score assessment after the operation. Patients were also permitted to remain on analgesics, non-steroidal anti-inflammatories and opioids during the course of treatment, which are likely to have confounded the results for all outcomes measured.	

STUDY DETAILS

Reference: Karow JH, Abt HP, Fröhling M, Ackermann H (2008). Efficacy of Arnica montana D4 for healing of wounds after Halluz valgus surgery compared to diclofenac. Journal of Alternative and Complementary Medicine 14: 17-25.

Affiliation/source of funds: Johann Wolfang Goethe-Universitat, Frankfurt, Germany
Conflicts of interest: not reported

Study design:	**Level of evidence:**	**Location/setting:**
Randomised, double-blind, parallel group study	Level II	Orthopaedic hospital in Frankfurt, Germany

Intervention:	**Comparator(s):**
Arnica D4, 10 pillules taken orally 3 times per day for 4 days postoperatively **Sample size:** n= 44	Diclofenac sodium, 50 mg taken orally 3 times per day for 4 days postoperatively **Sample size:** n= 44

Inclusion criteria: Men and women between the ages of 20 and 65 years with the surgical indication "*Hallux valgus"* or *"Hallux rigidus"* on the left and/or right metatarsal
Exclusion criteria: Clotting disorders (also due to low-dose acetylsalicylic acid), rheumatic diseases, serious metabolic disorders (e.g. diabetes mellitus), arterial occlusive disease, varicosis, lymphoedema, peptic ulcer, and elevated transaminase levels

***Population characteristics*:**
Baseline characteristics of study groups were not reported. The patient population consisted of men and women between the ages of 20 and 65 years with the surgical indication "Hallux valgus" or "Hallux rigidus" on the left and/or right metatarsal
Total study size: N=88

Length of follow-up: 4 days

INTERNAL VALIDITY

Allocation:	Comparison of study groups:	Blinding:	Treatment/ measurement bias:	Follow-up (ITT):
Method of randomisation unknown	Unclear risk of bias. No baseline characteristics for either study group were reported	Reported to be double-blind but it was not specifically mentioned if the patients or the assessors were blinded	Unclear	All 88 patients in the study were evaluated per protocol. No missing values were replaced

SIGN quality assessment (descriptive): Evidence level 1-. Most of the SIGN criteria have been fulfilled, however it is not addressed if the treatment and control groups are similar at the start of the trial. It is also poorly addressed if the only difference between groups is the treatment under investigation. These are critical confounding factors that may invalidate the results. There is thus a high risk of bias in this study.

RESULTS

Conclusions: "After foot operations, Arnica D4 can be used instead of diclofenac to reduce wound irritation"

Trial (N)	Intervention	Comparator	Outcome	Results (0.36 was the critical threshold for therapeutic equivalence)
Karow et al (2008) [Level II] *SIGN EL 1-* N=88	Arnica D4, 10 pillules taken orally 3 times per day for 4 days postoperatively	Diclofenac sodium, 50 mg taken orally 3 times per day for 4 days postoperatively	Postoperative wound irritation – rubor as measured by VAS	Arnica D3 and diclofenac are therapeutically equivalent • Lower margin of the 95% CI on day 4 is 0.4729; p=0.049
			Postoperative wound irritation – swelling as measured by VAS	Arnica D3 and diclofenac are therapeutically equivalent • Lower margin of the 95% CI on day 4 is 0.3674; p=0.58
			Postoperative wound irritation – calor as measured by VAS	Arnica D3 and diclofenac are therapeutically equivalent • Lower margin of the 95% CI on day 4 is 0.4106; p=0.89
			Patient mobility (as measured by patient questionnaire on how	Arnica D4 is not therapeutically inferior to diclofenac • Lower margin of the 95% CI on

			long he/she had been out of bed)	day 4 is 0.4726; p=0.045
			Pain as calculated by an area under the curve	Arnica D4 is therapeutically inferior to diclofenac • Lower margin of the 95% CI on day 4 is 0.2662; p=0.02
			Use of analgesics (Dipidolor, Tramal, Novalgin)	No significant difference between the groups
			Intolerance	Significant difference in favour of homeopathy (p=0.049) • Homeopathy group: 2/44 (4.5%) • Comparator group: 9/44 patients (20.45%)

Abbreviations: CI, confidence interval; ITT, intention to treat; SIGN, Scottish Intercollegiate Guidelines Network.

SIGN	**8 Methodology Checklist 2: Controlled Trials**

Study identification (*Include author, title, year of publication, journal title, pages*)

Karow JH, Abt HP, Fröhling M, Ackermann H (2008). Efficacy of Arnica montana D4 for healing of wounds after Halluz valgus surgery compared to diclofenac. Journal of Alternative and Complementary Medicine 14: 17-25.

Guideline topic: Effectiveness of homeopathy for a specific clinical condition	Key Question No: 1

Checklist completed by: OPTUM

SECTION 1: INTERNAL VALIDITY

	In a well conducted RCT study…	***9 In this study this criterion is:***
1.1	The study addresses an appropriate and clearly focused question.	Well covered
1.2	The assignment of subjects to treatment groups is randomised	Adequately addressed
1.3	An adequate concealment method is used	Adequately addressed
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Adequately addressed
1.5	The treatment and control groups are similar at the start of the trial	Not addressed
1.6	The only difference between groups is the treatment under investigation	Poorly addressed
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Adequately addressed
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	Homeopathy group: 2/44 patients (5%) Comparator group: 9/44 patients (20%) However, all 88 patients included in the study were evaluated per protocol. No missing values were replaced
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Not applicable. Per protocol analysis
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias? *Code ++, +, or –*	1- (downgraded from ++ as it was unclear if the participants were similar at the start of the trial, unclear if the only difference between groups in the treatment under investigation and intention-to-treat analysis was not performed
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	No, it is unclear if the patients remained on any other medications that may have influenced the primary outcomes. No baseline characteristics were provided, so it is also unclear if the study groups were similar at

		baseline.
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes
2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.	
	The authors found that Arnica D4 and diclofenac were equivalent for wound irritation and patient mobility. A descriptive analysis reported the superiority of Arnica D4 with respect to patient mobility. With respect to pain, Arnica D4 was inferior to diclofenac. No significant differences were found regarding the use of additional analgesics during the 4 postoperative days. Arnica D4 was significantly better tolerated than diclofenac. Overall, the authors concluded that after foot operations, Arnica D4 can be uased instead of diclofenace to reduce wound irritation. The evidence reviewer notes that outcomes may be subjected to a high risk of bias. Patient demographics were not provided and it was not addressed if the study groups were comparable at baseline. It is also unclear if the patients remained on any other medications that may have influenced the primary outcomes.	

STUDY DETAILS

Reference: Seeley BM, Denton AB, Ahn MS Maas CS (2006). Effect of homeopathic arnica montana on bruising in face-lifts. Archives of Facial Plastic Surgeons 8: 54-59.

Affiliation/source of funds: This study was supported in part by a research grant from Alpine Pharmaceuticals, makers of SINECCH

Conflicts of interest: Not reported

Study design:	**Level of evidence:**	**Location/setting:**
Randomised, double-blind, placebo-controlled trial	Level II	Tertiary care centre, location not reported

Intervention:	**Comparator(s):**
SINECCH (Arnica montana), once every 8 hours for 4 days **Sample size:** n=14	Placebo **Sample size:** n=15

Inclusion criteria: Patients undergoing elective rhytidectomy

Exclusion criteria: Not reported

Population characteristics

Patients undergoing elective rhytidectomy. All patients were white women who were non-smokers. They also denied having tendencies toward easy bleeding and bruising, using recent aspirin or nonsteroidal anti-inflammatory drugs and having undergone any previous facial surgical procedure.

Total study size: N=29

Length of follow-up: 10 days

INTERNAL VALIDITY

Allocation:	Comparison of study groups:	Blinding:	Treatment/ measurement bias:	Follow-up (ITT):
Patients were assigned study numbers and randomly given a regimen of either homeopathy or placebo in a double-blind fashion	Homeopathy vs placebo. Baseline demographics were not provided so it is unclear if the study groups were comparable at baseline	Double-blind.	Unclear risk of bias	3 patients did not complete the VAS.

SIGN quality assessment (descriptive): Evidence level 1-. Most of the SIGN criteria have been fulfilled, however it is poorly addressed if the treatment and control groups are similar at the start of the trial, and if the only difference between groups is the treatment under investigation. In addition, this study used a newly designed computer model to assess perioperative colour changes, both in terms of area and degree. This model has not been validated and confirmed as an appropriate means to make these assessments.

RESULTS

"The computer model provides an efficient, objective and reproducible means with which to assess perioperative colour changes, both in terms of area and degree. Patients taking perioperative homeopathic A Montana exhibited less ecchymosis, and that difference was statistically significant (P<0.05) on 2 of the 4 postoperative data points evaluated"

Trial (N) *Quality*	Intervention	Comparator	Outcome	Results
Seeley et al (2006) [Level II] *SIGN EL 1-* N=29	SINECCH (Arnica montana), once every 8 hours for 4 days postoperatively	Placebo	Subjective assessment by the patient using VAS	No significant difference
			Subjective assessment by the nurse/physician using VAS	No significant difference
			Degree of colour change attributable to surgery as measured by the computer model	No significant difference
			Reduction in ecchymosis as measured by the	Significant difference in favour of homeopathy only on postoperative days 1 (P<0.005)

			computer model	and 7 (P<0.001). No significant difference on postoperative days 5 and 10

Abbreviations: ITT, intention to treat; SIGN, Scottish Intercollegiate Guidelines Network; VAS, Visual analogue scale.

SIGN	**10 Methodology Checklist 2: Controlled Trials**

Study identification (*Include author, title, year of publication, journal title, pages*)

Seeley BM, Denton AB, Ahn MS Maas CS (2006). Effect of homeopathic arnica montana on bruising in face-lifts. Archives of Facial Plastic Surgeons 8: 54-59.

Guideline topic: Effectiveness of homeopathy for a specific clinical condition	Key Question No: 1

Checklist completed by: OPTUM

SECTION 1: INTERNAL VALIDITY		
In a well conducted RCT study…		***11 In this study this criterion is:***
1.1	The study addresses an appropriate and clearly focused question.	Well covered
1.2	The assignment of subjects to treatment groups is randomised	Adequately addressed
1.3	An adequate concealment method is used	Adequately addressed
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Adequately addressed
1.5	The treatment and control groups are similar at the start of the trial	Poorly addressed
1.6	The only difference between groups is the treatment under investigation	Poorly addressed
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Adequately addressed
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	3 patients did not complete the visual analogue scale for subjective evaluation Homeopathy group: 0/14 (0%) Placebo group: 3/15 (20%)
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Adequately addressed
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Not applicable
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise bias? *Code ++, +, or –*	1- (downgraded from ++ as it was unclear if the participants were similar at the start of the trial, unclear if the only difference between groups in the treatment under investigation and outcomes were measured using a computer model that had not been validated)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	No, the trial was small in size and it is unclear if the study groups were similar at baseline. In addition, the efficacy of homeopathic Arnica Montana was evaluated using a computerised model. This model had not been tested previously and thus its ability to objectively

		evaluate efficacy is uncertain.
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes
2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.	
	The authors found no subjective differences between the treatment and control group, either by the patients or by the professional staff. No objective difference in the degree of colour change was found. Patients receiving homeopathy were found to have a smaller area of ecchymosis on posteropative days 1, 5, 7 and 10. These differences were statistically significant only on postoperative days 1 and 7. The evidence reviewer notes that baseline demographics were not provided so it is unclear if the study groups were comparable at baseline. It is also unclear if the assessing nurse/physician was blinded to treatment allocation. Importantly, this study used a newly designed computer model to assess perioperative colour changes, both in terms of area and degree. This model has not been validated and confirmed as an appropriate means to make these assessments.	

STUDY DETAILS

Reference: Sinha MN, Siddiqui VA, Nayak C, Singh V, Dixit R, Dewan D, Mishra A (2012). Randomised controlled pilot study to compare Homeopathy and conventional therapy in Acute Otitis Media. Homeopathy 101: 5-12.

Affiliation/source of funds: Not reported
Conflicts of interest: Not reported

Study design:	**Level of evidence:**	**Location/setting:**
Randomised, double-blind, controlled trial	Level II	Regional Research Institute of Homeopathy, Jaipur, India

Intervention:	**Comparator(s):**
Individualised homeopathy in 50 LM potencies. If less than 50% improvement was observed in the first 3 days of treatment, antibiotics were given. However, the authors noted that no antibiotics were required for any case in the homeopathy group. **Sample size:** n=40	Conventional treatment. An 'observation option' was adopted for the first 3 days: patients were given symptomatic treatment without antibiotics (may include analgesics, anti-pyretic, anti-inflammatories). If less than 50% improvement was observed in the first 3 days of treatment, antibiotics were given. **Sample size:** n=41

Inclusion criteria: Children of both sexes, between 2 and 6 years of age. Earache of not more than 36 hours duration. Tympanic membrane bulging with loss of landmarks
Exclusion criteria: Patients having any discharge or history of discharge from ear; history of convulsions; subperiosteal abscess of mastoid; grossly deviated nasal septum; suspected enlarged adenoids; Otitis Media with effusion; on antibiotics in the past 7 days or on steroid therapy; suffering from any systemic disease

Population characteristics
Intervention and comparator group: Children with earache of not more than 36 hours duration. Mean age 4±2 years; 50% male and 50% females
Total study size: N=81

Length of follow-up: 21 days

INTERNAL VALIDITY

Allocation:	Comparison of study groups:	Blinding:	Treatment/ measurement bias:	Follow-up (ITT):
Adequate random sequence generation. Allocation concealment not described.	Homeopathy vs active comparator. No significant differences in baseline characteristics between groups	Double-blind	Unclear risk of bias	1 patient in comparator group lost to follow up

SIGN quality assessment (descriptive): Evidence Level 1+. All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study are thought very unlikely to alter.

RESULTS

Overall conclusion: "Individualised homeopathy is an effective conventional outcome in acute otitis media. There were no significant differences between groups in the main outcome. Symptomatic improvement was quicker in the homeopathy group and there was a large difference in antibiotic requirements favouring homeopathy"

Trial (N)	Intervention	Comparator	Outcome	Results
Sinha et al (2012) [Level II] *SIGN EL 1+* N=81	Individualised homeopathy in 50LM potencies	Conventional therapy An 'observation option' was adopted for the first 3 days: patients were given symptomatic treatment without antibiotics (may include analgesics, anti-pyretic, anti-inflammatories). If less than 50% improvement was observed in the first 3 days of treatment, antibiotics were given.	Cured on the 3rd day	Significant difference in favour of homeopathy (p=0.000) • Homeopathy group: 4/40 (10%) • Comparator group: 1/40 (2.5%)
			Cured on the 7th, 10th or 21st day	No significant difference
			Symptomatic improvement	No significant difference

Abbreviations: EL, evidence level; LM, Millesimal scale; ITT, intention to treat; SIGN, Scottish Intercollegiate Guidelines Network.

SIGN	**12 Methodology Checklist 2: Controlled Trials**

Study identification (*Include author, title, year of publication, journal title, pages*)

Sinha MN, Siddiqui VA, Nayak C, Singh V, Dixit R, Dewan D, Mishra A (2012). Randomised controlled pilot study to compare Homeopathy and conventional therapy in Acute Otitis Media. Homeopathy 101: 5-12.

Guideline topic: Effectiveness of homeopathy for a specific clinical condition	Key Question No: 1

Checklist completed by: OPTUM

SECTION 1: INTERNAL VALIDITY

In a well conducted RCT study…		***13 In this study this criterion is:***
1.1	The study addresses an appropriate and clearly focused question.	Well covered
1.2	The assignment of subjects to treatment groups is randomised	Well covered
1.3	An adequate concealment method is used	Not addressed
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Adequately addressed
1.5	The treatment and control groups are similar at the start of the trial	Well covered
1.6	The only difference between groups is the treatment under investigation	Adequately addressed
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Adequately addressed
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	Homeopathy group: 2/40 patients (5%) did not complete the last two follow ups but they were considered under the last observation carried forward principle Comparator group: 1/40 patients (3%)
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias? *Code ++, +, or –*	1+ (downgrade from ++ as allocation concealment was not described)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	10 different homeopathic medicines were prescribed across the 40 patients in the treatment group.
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes

2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.
	The authors concluded that "individualised homeopathy is an effective conventional outcome in acute otitis media. There were no significant differences between groups in the main outcome. Symptomatic improvement was quicker in the homeopathy group and there was a large difference in antibiotic requirements favouring homeopathy."

STUDY DETAILS

Reference: Tveiten D, Bruset S, Borchgrevink CF, Norseth J (1998). Effects of the homoeopathic remedy Arnica D30 on marathon runners: a randomised, double-blind study during the 1995 Oslo marathon. Complementary Therapies in Medicine 6:71-74.

Affiliation/source of funds: Norwegian Research Council funded the study. Homeopathic drugs and corresponding placebo pills were supplied free of charge by Biomedica Nordern AB, Sweden
Conflicts of interest: Not reported

Study design:	**Level of evidence:**	**Location/setting:**
Randomised, double-blind, placebo-controlled trial	Level II	Oslo marathon, September 1995

Intervention:	**Comparator(s):**
Arnica D30, 5 pills in the evening before the marathon and continued the morning and evening on the day of the run and for the following 3 days **Sample size:** n=24	Placebo **Sample size:** n=22

Inclusion criteria: Participants entering the 1995 Oslo marathon
Exclusion criteria: Not reported

Population characteristics
Intervention group: mean age 38 (range 37-52); mean total number of marathons 10.2 (range 0-50); mean running each week 51.3 km (range 20-100 km)
Comparator group: mean age 41 (range 31-50); mean total number of marathons 12.3 (range 1-31); mean running each week 46.1 km (range 15-85 km)
Total study size: N=71 included in the trial, N=46 evaluated

Length of follow-up: 3 days

INTERNAL VALIDITY

Allocation:	Comparison of study groups:	Blinding:	Treatment/ measurement bias:	Follow-up (ITT):
Low risk of bias. Participants randomised in blocks using a computer algorithm	Homeopathy vs placebo. "The baseline of the runners show no important difference between the groups"	Low risk of bias. Randomisation code was unsealed after analysis of all data	Low risk of bias. Muscle soreness assessed by VAS. Cell damage assessed by routine blood screening tests	46 runners completed the trial - 5 runners dropped out 1 week before the marathon. 20 runners dropped out the day before and same day as the marathon

SIGN quality assessment (descriptive): Evidence level 1+. Most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study are thought unlikely to alter the conclusions.

RESULTS

Overall conclusion: "In this study, Arnica D30 had a positive effect on muscle soreness after marathon running, but not on cell damage as measured by enzymes."

Trial (N) *Quality*	Intervention	Comparator	Outcome	Results
Tveiten et al (1998) [Level II] *SIGN EL 1+* N=71	Arnica D30, 5 pills in the evening before the marathon and continued the morning and evening on the day of the run and for the following 3 days	Placebo	Muscle soreness immediately after the marathon as measured by VAS	Significantly lower in the Arnica group compared with placebo (p=0.017)
			Mean estimated muscle soreness for the entire treatment period as measured by VAS	No significant difference
			Cell damage measured by enzymes	No difference between the two groups
			Electrolytes and	No difference between the two

			creatinine	groups
			Side effects	No side effects were reported in either group

Abbreviations: D, Decimal scale; EL, Evidence level; ITT, intention to treat; SIGN, Scottish Intercollegiate Guidelines Network; VAS, Visual analogue scale.

SIGN	**14 Methodology Checklist 2: Controlled Trials**

Study identification (*Include author, title, year of publication, journal title, pages*)

Tveiten D, Bruset S, Borchgrevink CF, Norseth J (1998). Effects of the homoeopathic remedy Arnica D30 on marathon runners: a randomised, double-blind study during the 1995 Oslo marathon. Complementary Therapies in Medicine 6:71-74.

Guideline topic: Effectiveness of homeopathy for a specific clinical condition	Key Question No: 1

Checklist completed by: OPTUM

SECTION 1: INTERNAL VALIDITY

In a well conducted RCT study…		***15 In this study this criterion is:***
1.1	The study addresses an appropriate and clearly focused question.	Well covered
1.2	The assignment of subjects to treatment groups is randomised	Well covered
1.3	An adequate concealment method is used	Well covered
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Well covered
1.5	The treatment and control groups are similar at the start of the trial	Adequately addressed
1.6	The only difference between groups is the treatment under investigation	Adequately addressed
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Well covered
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	5 patients dropped out of the trial 1 week before the marathon from unknown study arms. 20 patients dropped out of the trial one day before or on the day of the marathon as follows: Homeopathy group: 9/33 (27%) Placebo group: 11/33 (33%)
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias? *Code ++, +, or –*	Evidence level 1+ (downgraded from 1++ due to high loss to follow up)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	Overall, this study was of good methodological quality and the two study groups were similar at baseline. However, a potential confounding factor that was not addressed is if the participants were permitted to consume other substances (e.g. sports drinks) that may have an effect on their recovery and the results of the

		trial.
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes
2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.	
	The authors found that muscle soreness was significantly lower in the Arnica group than in the placebo group immediately after the marathon (p=0.017). Cell damage measured by enzymes was essentially the same whether the runners were treated with Arnica D30 or placebo. The authors concluded Arnica D30 had a positive effect on muscle soreness after marathon running, but not on cell damage as measured by enzymes. However, the evidence reviewer notes that a potential confounding factor that was not addressed is if the participants were permitted to consume other substances (e.g. sports drinks) that may have an effect on their recovery and the results of the trial.	

STUDY DETAILS

Reference: Vickers A, Fisher P, Smith C, Wyllie SE, Lewith GT (1998). Arnica 30X is ineffective for muscle soreness after long-distance running: a randomised, double-blind, placebo controlled trial. Clinical Journal of Pain 14: 227-231.

Affiliation/source of funds: Blackie Foundation Trust
Conflicts of interest: Not reported

Study design:	**Level of evidence:**	**Location/setting:**
Randomised, double-blind, placebo-controlled trial	Level II	Long distance runs taking place in the community

Intervention:	**Comparator(s):**
Arnica Montana 30X, 5 pills twice daily starting the evening before the race and continuing until 9 doses had been taken **Sample size:** n=200	Placebo **Sample size:** n=200

Inclusion criteria: Aged 18 years and over; Must have experienced delayed onset muscle soreness following a run of similar or lesser length and difficulty to the forthcoming race or have a good reason to expect that they would do so
Exclusion criteria: No exclusion criteria

Population characteristics
Intervention group: Mean age 42.5±11.1; 156 males and 44 females
Comparator group: Mean age 42.4±10.0 (2 missing observations); 138 male and 62 female
Total study size: N=400

Length of follow-up: 5 days

INTERNAL VALIDITY

Allocation:	Comparison of study groups:	Blinding:	Treatment/ measurement bias:	Follow-up (ITT):
Low risk of bias. Adequate random sequence allocation and allocation concealment	Homeopathy vs placebo. Groups were well matched at baseline, apart from a slightly higher number of women among controls	Double-blind	Low risk of bias	27 participants lost to follow up

SIGN quality assessment (descriptive): Evidence level 1++. All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought very unlikely to alter.

RESULTS

Overall conclusion: "Homeopathic Arnica 30X is ineffective for muscle soreness following long-distance running" and "Arnica 30X does not reduce delayed onset muscle soreness resulting from long-distance running. Homeopaths should not prescribe Arnica for this indication, and runners should be advised not to take it."

Trial (N)	Intervention	Comparator	Outcome	Results
Vickers et al (1998) [Level II] *SIGN EL1+* N=400	Arnica Montana 30X, 5 pills twice daily starting the evening before the race and continuing until 9 doses had been taken	Placebo	Mean 2-day Visual Analogue Scale for soreness	No significant difference
			Likert score for soreness	No significant difference
			Race time	No significant difference

Abbreviations: EL, evidence level; ITT, intention to treat; SIGN, Scottish Intercollegiate Guidelines Network.

SIGN	**16 Methodology Checklist 2: Controlled Trials**

Study identification (*Include author, title, year of publication, journal title, pages*)

Vickers A, Fisher P, Smith C, Wyllie SE, Lewith GT (1998). Arnica 30X is ineffective for muscle soreness after long-distance running: a randomised, double-blind, placebo controlled trial. Clinical Journal of Pain 14: 227-231.

Guideline topic: Effectiveness of homeopathy for a specific clinical condition	Key Question No: 1

Checklist completed by: OPTUM

SECTION 1: INTERNAL VALIDITY

In a well conducted RCT study…		***17 In this study this criterion is:***
1.1	The study addresses an appropriate and clearly focused question.	Well covered
1.2	The assignment of subjects to treatment groups is randomised	Well covered
1.3	An adequate concealment method is used	Well covered
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Well covered
1.5	The treatment and control groups are similar at the start of the trial	Adequately addressed
1.6	The only difference between groups is the treatment under investigation	Adequately addressed
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Adequately addressed
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	Homeopathy group: 13/200 (7%) Placebo group: 14/200 (7.0%)
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Not addressed

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias? *Code ++, +, or –*	1++
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	Overall, this study was of good methodological quality and the two study groups were similar at baseline. However, a potential confounding factor that was not addressed is if the participants were permitted to consume other substances (e.g. sports drinks) that may have an effect on their recovery and the results of the trial.
2.3	Are the results of this study directly applicable to the	Yes

	patient group targeted by this guideline?	
2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.	
	The authors concluded that "Homeopathic Arnica 30X is ineffective for muscle soreness following long-distance running" and "Arnica 30X does not reduce delayed onset muscle soreness resulting from long-distance running. Homeopaths should not prescribe Arnica for this indication, and runners should be advised not to take it"	

STUDY DETAILS

Reference: Waldschütz R, Klein P (2008). The homeopathic preparation Neurexan vs. valerian for the treatment of insomnia: an observational study. Scientific World Journal 8: 411-420.

Affiliation/source of funds: Not reported
Conflicts of interest: Not reported

Study design:	**Level of evidence:**	**Location/setting:**
Open label, prospective cohort study	Level III-2	89 German centres offering both conventional and complementary therapies

Intervention:	**Comparator(s):**
Homeopathic Neurexan® for 28 days. Dosage at physician's judgements **Sample size:** n=197	Valerian. Dosage at physician's judgement **Sample size:** n=212

Inclusion criteria: Participants aged 18–75 years and a verified condition of mild to moderate sleep onset and/or sleep maintenance insomnias (sleep latency, low sleep quality, frequent nocturnal awakenings, sleep-associated impaired quality of life) diagnosed no longer than 4 weeks prior to enrolment. The conditions could be newly diagnosed or recurring. A minimum of three nights of insomnias a week was necessary, and the sleep disturbances were to have a significant negative impact on subjects' social and professional lives
Exclusion criteria: Presence of concomitant diseases and intolerance to any of the study medications or their components

Population characteristics
Patients with mild to moderate sleep onset and/or sleep maintenance insomnias
Intervention group: Mean age 50.5±14.1 years; 77% women
Comparator group: Mean age 50.1±14.7 years; 68% women
Total study size: N=409

Length of follow-up: 28 days

INTERNAL VALIDITY

Allocation:	Comparison of study groups:	Blinding:	Treatment/ measurement bias:	Follow-up (ITT):
Not applicable. Open label, prospective cohort study	Homeopathy vs active comparator. Treatment groups were balanced at baseline for age, sex, weight and the manifestations of the sleep disturbances	Open-label	Risk of assessor bias	41/197 (21%) in homeopathy group and 48/212 (23%) in comparator group did not adhere to the protocol and were excluded

SIGN quality assessment (descriptive): Evidence level 2-. Few or no criteria fulfilled. The conclusions of the study are thought likely or very likely to alter.

RESULTS

- Neurexan was non-inferior to valerian on all variables assessed
- Overall conclusion: "For patients favourable towards a CAM-based therapy, Neurexan might be an effective and well-tolerated alternative to conventional valerian-based therapies for the treatment of mild to moderate insomnia. The results suggest greater short-term effects with Neurexan on sleep duration and on daytime fatigue after 1 month of treatment"

Trial (N)	Intervention	Comparator	Outcome	Results
Waldschutz and Klein (2008) [Level III-2] *SIGN EL 2-* N=409	Homeopathic Neurexan® for 28 days. Dosage at physician's judgements	Valerian. Dosage at physician's judgement	Improvements in sleep latency after 14 days' treatment	No significant difference between groups
			Duration of sleep after 14 days' treatment (measured daily)	Significantly favoured Neurexan therapy at days 8, 12 and 14 (P-value not reported) • Homeopathy group: duration increased by 2.2±1.6 hours • Comparator group: duration increased by 2.0±1.5 hours
			Sleep quality at day 28	No significant difference between groups
			Daytime fatigue	Significant improvement in favour of Neurexan (P<0.05) • Homeopathy group: 49%

				reported no daytime fatigue • Comparator group: 32% reported no daytime fatigue
			Time of first signs of improvement	No significant difference between groups
			Overall effectiveness	No significant difference between groups
			Overall symptomatic change since beginning of therapy	No significant difference between groups
			Adverse event	1 case of mild caffeine intolerance associated with Neurexan after 9 days of treatment
			Mean blood pressure	No significant differences between groups
			Compliance rate	No significant differences between groups

Abbreviations: CAM, complementary and alternative medicine; EL, Evidence level; ITT, intention to treat; SIGN, Scottish Intercollegiate Guidelines Network.

SIGN	**Methodology Checklist 3: Cohort studies**

Study identification (*Include author, title, year of publication, journal title, pages*)

Waldschütz R, Klein P (2008). The homeopathic preparation Neurexan vs. valerian for the treatment of insomnia: an observational study. Scientific World Journal 8: 411-420.

Guideline topic: Effectiveness of homeopathy for a specific clinical condition	Key Question No: 1

Checklist completed by: OPTUM

SECTION 1: INTERNAL VALIDITY

In a well conducted cohort study:		***18 In this study the criterion is:***
1.1	The study addresses an appropriate and clearly focused question.	Well covered
SELECTION OF SUBJECTS		
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Well covered
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Well covered
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Not addressed
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed.	Homeopathy group: 41/197 (21%) Comparator group: 48/212 (23%)
1.6	Comparison is made between full participants and those lost to follow up, by exposure status.	Poorly addressed
ASSESSMENT		
1.7	The outcomes are clearly defined.	Well covered
1.8	The assessment of outcome is made blind to exposure status.	Not applicable
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.	Not addressed
1.10	The measure of assessment of exposure is reliable.	Adequately addressed
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.	Not addressed
1.12	Exposure level or prognostic factor is assessed more than once.	Well covered
CONFOUNDING		
1.13	The main potential confounders are identified and	Not addressed

	taken into account in the design and analysis.	
STATISTICAL ANALYSIS		
1.14	Have confidence intervals been provided?	No
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding, and to establish a causal relationship between exposure and effect? *Code ++, +, or –*	2- (study design was not suitable to investigate non-inferiority and high loss to follow up)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	No, the open-label cohort design introduces a bias and is not the best study type to examine the effectiveness of Neurexan on patients with insomnia
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes
2.4	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question. Overall, the authors concluded that "for patients favourable towards a CAM-based therapy, Neurexan might be an effective and well-tolerated alternative to conventional valerian-based therapies for the treatment of mild to moderate insomnia. The results suggest greater short-term effects with Neurexan on sleep duration and on daytime fatigue after 1 month of treatment".	