



Australian Government
National Health and Medical Research Council

N|H|M|R|C

NHMRC INFORMATION PAPER

Evidence on the effectiveness of
homeopathy for treating health conditions

March 2015

Publication Details

Publication title:	NHMRC Information Paper: Evidence on the effectiveness of homeopathy for treating health conditions
Published:	March 2015
Publisher:	National Health and Medical Research Council
NHMRC Publication reference:	CAM02A
Online version:	www.nhmrc.gov.au/guidelines-publications/cam02
ISBN Online:	978-1-925129-29-8
Suggested citation:	National Health and Medical Research Council. 2015. <i>NHMRC Information Paper: Evidence on the effectiveness of homeopathy for treating health conditions</i> . Canberra: National Health and Medical Research Council; 2015

Copyright

© Commonwealth of Australia 2015



All material presented in this publication is provided under a Creative Commons Attribution 3.0 Australia licence (<http://creativecommons.org.au>), with the exception of the Commonwealth Coat of Arms, NHMRC logo and content identified as being owned by third parties. The details of the relevant licence conditions are available on the Creative Commons website (<http://creativecommons.org.au>), as is the full legal code for the CC BY 3.0 AU licence.

Attribution

Creative Commons Attribution 3.0 Australia Licence is a standard form license agreement that allows you to copy, distribute, transmit and adapt this publication provided that you attribute the work. The NHMRC's preference is that you attribute this publication (and any material sourced from it) using the following wording: Source: National Health and Medical Research Council.

Use of images

Unless otherwise stated, all images (including background images, icons and illustrations) are copyrighted by their original owners.

Contact us

To obtain information regarding NHMRC publications or submit a copyright request, contact:

E: nhmrc.publications@nhmrc.gov.au

P: 13 000 NHMRC (13 000 64672)

or call (02) 6217 9000

Contents

About NHMRC	4
Executive summary	5
Homeopathy	5
Methods	5
Findings	6
Conclusions	6
Introduction	7
Purpose	7
Scope	7
What is homeopathy?	7
Why did NHMRC conduct an assessment of homeopathy?	8
NHMRC's approach to assessing health evidence	9
About NHMRC's assessment of the evidence	11
Sources of information	11
How did NHMRC assess the evidence about homeopathy?	14
What quality checks were applied to NHMRC's assessment of the evidence on homeopathy?	15
Findings of the NHMRC assessment of the evidence	16
Overview	16
Information provided by homeopathy interest groups and individuals	21
Overall findings based on the evidence	24
Limitations of the assessment and evidence base for homeopathy	25
NHMRC's interpretation of the assessment of the evidence on the effectiveness of homeopathy	27
Definition of special terms	28
Appendix A. NHMRC evidence hierarchy, including explanatory notes	30
Explanatory notes	30
Appendix B. The Homeopathy Working Committee	31
Appendix C. Criteria for the development of evidence statements	33
Purpose and role of the criteria	33
Introduction to the criteria	33
References	39

About NHMRC

NHMRC is Australia's peak body for supporting health and medical research by funding the best research, selected through a competitive peer review process. NHMRC also develops health advice for the Australian community, health professionals and governments in the form of public health and clinical practice guidelines, Statements, Information Papers and evidence reviews. NHMRC also provides advice on ethical behaviour in health care and in the conduct of health and medical research.

The work of NHMRC is guided by its Strategic Plan, and defined by the *National Health and Medical Research Council (NHMRC) Act 1992*. The Strategic Plan covers a three year period and is submitted to the Health Minister for approval, prior to being tabled in Parliament. The NHMRC Strategic Plan 2013–2015^[1] has identified 'claiming benefit for human health not based on evidence' as a major health issue for consideration.

This Information Paper is an example of NHMRC's function to 'advise the community' under section 7(1)(a) of the *NHMRC Act 1992*. Published research on a topic of interest has been identified, analysed and synthesised into a summary of the evidence for the Australian community, health professionals and policy makers. This information can then be utilised to assist people in making healthcare choices, guide clinical practice or influence policy and perhaps new funding approaches, all of which lead to improvements in health and health care delivery.

Within our health system, there are practices which are currently not based on sturdy evidence. Health and medical research is the means by which we test the value of procedures, processes, systems and products offered to patients, or proposed as preventive means by the health system and its policy and decision makers.

NHMRC is a strong advocate for the development and use of evidence to inform policy and practice and in recent years, NHMRC and other health research funding bodies have increased funding for such research.

NHMRC is of the view that when offering treatments for illness, all registered health practitioners must give consideration to the evidence for the effectiveness of such treatments. This consideration should be reflected in their professional ethics and clinical practices.

Executive summary

Homeopathy

Homeopathy is a type of complementary and alternative medicine that is commonly used in Australia and around the world. It is based on two premises:

- that substances that may cause illness or symptoms in a healthy person can, in very small doses, treat those symptoms in a person who is unwell, and
- that highly diluted preparations retain a ‘memory’ of the original substance. Homeopathic medicines are prepared by taking a substance (e.g. plant, animal material, or chemical), diluting it in water or alcohol, then forcefully hitting the container against a hand or a surface. This process is repeated several times.

Homeopathic medicines include pellets placed under the tongue, tablets, liquids, ointments, sprays and creams.

Methods

The National Health and Medical Research Council (NHMRC) undertook an assessment of the evidence of the effectiveness of homeopathy. This assessment was based on:

- an overview of published systematic reviews by an independent contractor^[2],
- an independent evaluation of information provided by homeopathy interest groups and the public^[3, 4], and
- consideration of clinical practice guidelines and government reports on homeopathy published in other countries.

The assessment of the evidence used standardised, accepted methods for assessing the quality and reliability of evidence for whether or not a therapy is effective for treating health conditions.

This work was overseen by the Homeopathy Working Committee established by the NHMRC. Given their collective expertise in evidence-based medicine, study design, and complementary and alternative medicine research, the Homeopathy Working Committee also provided advice on how the evidence should be interpreted in developing an Information Paper. An approach, similar to that of a Health Technology Assessment, was used to consider the outcomes of the assessment of the evidence. This means that for a treatment to be considered effective, it must result in health improvements that cannot be explained by the placebo effect, and these health improvements must be meaningful for a person’s overall health. There must be evidence that the health improvements in people taking the treatment are unlikely to be due to chance and the result must be seen consistently in several studies.

Evidence on homeopathy was collected by identifying systematic reviews which evaluated the effectiveness of homeopathy in treating health conditions in humans. In total, 57 systematic reviews were identified that contained 176 individual studies. Studies were only considered by NHMRC if they compared a group of people who were given homeopathic treatment with a similar group of people who were not given homeopathic treatment (controlled studies). For each health condition, the evidence reviewers assessed the quality of the systematic reviews using a standard, internationally

accepted method, and recorded the number and type of studies that were included in the systematic reviews. Using the information provided by the systematic reviews, the reviewers also assessed the quality of each individual study and its number of participants, taking into account factors that could bias the results in favour of homeopathy, placebo or another treatment.

Additional information was submitted to NHMRC, for consideration as part of its review of homeopathy, by homeopathy interest groups and the public on two occasions: before the commissioned overview of evidence (preliminary submitted literature) and during the review of the draft Information Paper (public consultation submitted literature). The preliminary and public consultation submitted literature was assessed using a similar method to that applied in the overview.

Where a clinical condition had already been considered in the overview, the results from the submitted literature were compared to the conclusions of the overview to examine the consistency of results against the body of evidence. Where a clinical condition had not been considered in the overview, the results of the submitted literature were assessed with regards to their study design, size and different kinds of bias to see if any comment on the effectiveness of homeopathy could be made.

Findings

There was no reliable evidence from research in humans that homeopathy was effective for treating the range of health conditions considered: no good-quality, well-designed studies with enough participants for a meaningful result reported either that homeopathy caused greater health improvements than placebo, or caused health improvements equal to those of another treatment.

For some health conditions, studies reported that homeopathy was not more effective than placebo. For other health conditions, there were poor-quality studies that reported homeopathy was more effective than placebo, or as effective as another treatment. However, based on their limitations, those studies were not reliable for making conclusions about whether homeopathy was effective. For the remaining health conditions it was not possible to make any conclusion about whether homeopathy was effective or not, because there was not enough evidence.

Conclusions

Based on the assessment of the evidence of effectiveness of homeopathy, NHMRC concludes that there are no health conditions for which there is reliable evidence that homeopathy is effective.

Homeopathy should not be used to treat health conditions that are chronic, serious, or could become serious. People who choose homeopathy may put their health at risk if they reject or delay treatments for which there is good evidence for safety and effectiveness. People who are considering whether to use homeopathy should first get advice from a registered health practitioner. Those who use homeopathy should tell their health practitioner and should keep taking any prescribed treatments.

Introduction

Purpose

This Information Paper provides a summary of evidence from research on the effectiveness of homeopathy in treating health conditions in humans.

Scope

NHMRC assessed the evidence on homeopathy to answer this question: *Is homeopathy an effective treatment for health conditions, compared with no homeopathy, or compared to other treatments?*

NHMRC did not consider any of these types of evidence:

- laboratory studies;
- studies in animals;
- studies in humans without a specific health condition, including:
 - studies investigating whether or not homeopathy is effective for preventing health conditions;
 - evidence about homeopathic ‘vaccines’; and
 - whether homeopathy is good for general health and wellbeing.

The focus of the assessment of the evidence was on the effectiveness of homeopathic medicines, not their safety.

What is homeopathy?

Homeopathy is a type of complementary and alternative medicine. It is based on two premises:

- that substances that may cause illness or symptoms in a healthy person can, in very small doses, treat those symptoms in a person who is unwell (‘like cures like’); and
- that highly diluted preparations retain a ‘memory’ of the original substance.

Homeopathic medicines are prepared by taking a substance (e.g. plant, animal material, or chemical) and repeatedly diluting it in water or alcohol. The container holding the preparation is then forcefully hit against a hand or a surface in a process known as ‘potentiation’ or ‘dynamisation’. Homeopathic medicines can include pellets placed under the tongue, tablets, liquids, ointments, sprays and creams.

Homeopaths provide either ‘individualised homeopathy’ or ‘clinical homeopathy’. In individualised homeopathy, the homeopath matches all the person’s symptoms to a single homeopathic medicine, rather than treating the person for a particular health condition using one or more homeopathic medicines. In clinical homeopathy, the homeopath chooses one or more homeopathic medicines to treat a particular health condition.

Homeopathy is commonly used around the world, however, there are no reliable estimates of Australians' current use of homeopathic medicines. A 2009 World Health Organisation review on the safety of homeopathy reported that each year, Australians spend an estimated US \$7.3 million on homeopathic medicines.^[5]

Why did NHMRC conduct an assessment of homeopathy?

NHMRC is responsible for supporting health and medical research as well as providing Australians with advice based on the best available evidence. This advice assists people in making informed decisions about their health care. This includes providing advice about the use of conventional therapies, as well as complementary and alternative medicines or traditional practices which, despite their longstanding history of use, may not have been demonstrated to be effective.

Many health care practices and products are promoted as beneficial to health when there is little or no evidence to support these claims. In some cases these claims may mislead people to reject practices and treatments that are proven to be effective, in favour of non-evidence-based treatments.

People who use homeopathy need to understand the potential benefits and risks to enable them to make an informed decision. Health practitioners also need to know what homeopathy is, be aware of the current scientific evidence from research on homeopathy, and understand any possible benefits and risks to patients—particularly when people decide to use homeopathy instead of other evidence-based treatments.

For these reasons, NHMRC undertook an assessment of the evidence to provide Australians with reliable information on the effectiveness of homeopathy.

NHMRC's approach to assessing health evidence

When assessing the effectiveness of treatments for health conditions, not all evidence has equal value.

It is not possible to tell whether a health treatment is effective or not simply by considering individuals' experiences or healthcare practitioners' beliefs. One reason personal testimonials are not reliable is that people may experience health benefits because they believe that a treatment is effective. This is known as the 'placebo effect'. Another reason is that healthcare practitioners cannot always tell whether changes in a person's health condition are due to the treatment or some other reason. For these reasons, medicines must be tested in a planned, structured scientific research project designed to prevent these kinds of experiences giving the false impression that a medicine is more or less effective than it really is.

Some types of studies provide stronger evidence than others because of how they are designed. If studies are poorly designed, there is a risk that results may be biased; that is, the results may under or over-estimate the real effect of the treatment being tested. Researchers have developed particular ways of designing studies that aim to minimise the potential for such bias. Reliable information about whether a particular medicine is effective for treating a health condition or not, comes from studies in which:

- the medicine is compared with a substance that has no effect (placebo) in a group of people with the health condition (placebo-controlled trial), or the medicine is compared with an effective standard treatment (controlled trial);
- each participant is given either the medicine or the placebo/other treatment at random (randomised trial);
- participants do not know whether they are taking the medicine or the placebo/other treatment, and researchers do not know which participants are taking each treatment, until the study is finished (double-blinded trial);
- there are enough participants to be reasonably confident that, if there is a bigger change in the health condition in one group compared to another, this is not just due to chance; and
- the correct statistical methods are used to analyse the results.

When treatments are intended to be adjusted for the individual patient (e.g. different doses or combinations of medicines), it is still necessary to test whether the medicine is effective or not. It is possible to design high-quality studies to assess treatment approaches that involve individualisation, such as homeopathy.

Even where researchers take care to design studies in a way that minimises bias, there is a chance that the results will show a statistically significant difference in favour of a treatment, when there is actually no effect. Therefore, the results of individual studies need to be repeated in other independent studies, to make sure the effects seen were not just due to chance. The most reliable information comes from research that combines the results of all available similar studies and analyses the results together (systematic reviews).

When evaluating health evidence and drafting health advice, NHMRC uses a rigorous approach that has been developed by Australian experts in research methods.^[6] Under the NHMRC system, there are different levels of evidence, ranging from level one (highest level, strongest evidence) to level four (lowest level, weakest evidence).^[7] Further detail about this hierarchy is provided at Appendix A.

The level of evidence assigned to each study design is based on the extent to which each study design is expected to minimise bias. The level of evidence is used to decide how much a study's results should be relied upon, when judging the overall evidence.

A treatment is considered effective for treating a health condition if it meets all of these key criteria:

- the treatment causes health improvements that cannot be explained by the placebo effect;
- health improvements that occur in people taking the treatment are unlikely to be due to chance;
- the health improvements caused by the treatment are meaningful for a person's overall health; and
- the health improvement occurs consistently in several studies.

About NHMRC's assessment of the evidence

Sources of information

The NHMRC assessment of the evidence used a combination of three main sources of information about the effectiveness of homeopathy (Figure 1):

- an evidence review (the 'overview of systematic reviews'), comprising a systematic review of published systematic reviews (summarised in the Overview report)^[2];
- evidence provided by homeopathy interest groups and the public at the beginning of the process, before the commissioned overview of evidence (preliminary submitted literature) and during review of the draft Information Paper (public consultation submitted literature).^[3, 4]
- evidence-based clinical practice guidelines, government reports on homeopathy published in other countries, and other reports.

The NHMRC's assessment was guided by a committee of experts in evidence evaluation, the Homeopathy Working Committee, appointed in April 2012 (Appendix B).

Overview of systematic reviews

Many systematic reviews of homeopathy studies have already been published. NHMRC commissioned a professional research group OptumInsight (Optum) to do a thorough search of published research to find systematic reviews of studies (prospective, controlled studies) that compared homeopathy with no homeopathy or with other treatments and measured effectiveness in patients with any health condition.

The researchers searched databases of health publications to find systematic reviews published in English between 1 January 1997 and 3 January 2013.

For each health condition, the research group collated the findings of the systematic reviews and assessed the quality and reliability of the evidence. The findings are described in detail in the Overview Report.^[2]

The purpose of this approach was to use published systematic reviews as a way of identifying the body of evidence for homeopathic treatments. The professional research group did not accept the conclusions or interpretations of the systematic reviews, but instead considered the included studies. The professional research group evaluated the quality of each of the included studies (Appendix C), using the information provided by the systematic reviews. This process had some limitations as well as strengths (see Limitations of the assessment and evidence base for homeopathy).

Evidence provided by homeopathy interest groups and individuals

Additional information was submitted by homeopathy interest groups and the public to NHMRC, for its consideration as a part of its review of homeopathy, on two occasions. The preliminary submitted literature on the effectiveness of homeopathy was provided by the Australian Homoeopathy Association and the Australian Medical Fellowship of Homeopathy as well as members of the public. During public consultation on the draft Information Paper, a range of stakeholders submitted

additional literature for consideration in the development of this Information Paper (public consultation submitted literature).

All submitted literature was assessed by independent contractors to identify evidence within the scope of NHMRC's assessment. Only the types of studies that were included in the overview (prospective, controlled studies) were assessed in detail. For each study included, the independent contractors assessed the quality and reliability of the results and summarised the findings in a review of submitted literature.^[3, 4]

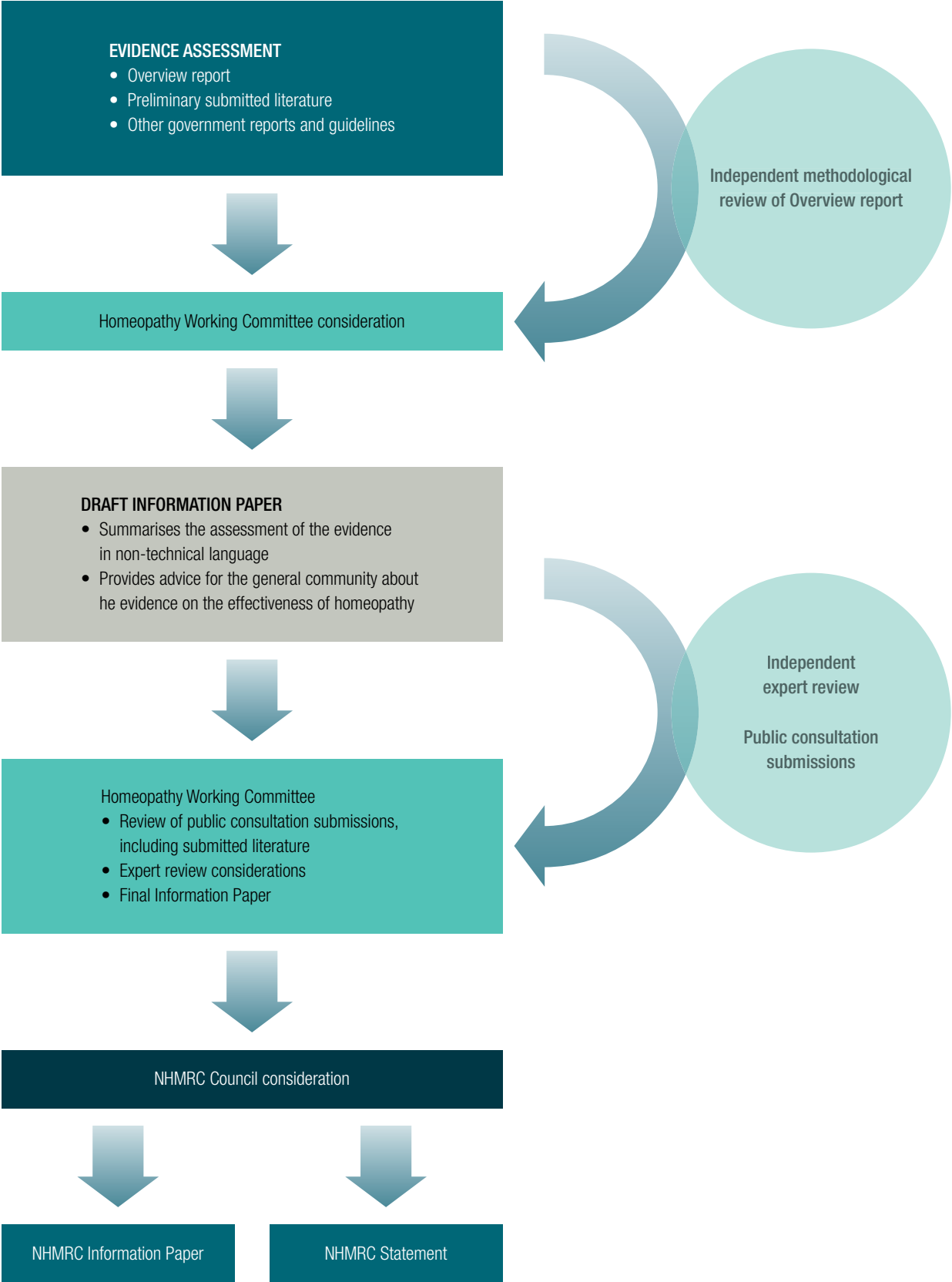
This evidence was considered when preparing this Information Paper.

Evidence-based guidelines, government reports

NHMRC identified a small number of relevant, recent European reports and guidelines which were considered when developing this Information Paper:

- a major United Kingdom Government report^[8]
- several evidence-based clinical practice guidelines,^[9-14] published or funded by the United Kingdom National Institute for Health and Clinical Excellence, which included recommendations about the use of homeopathy in the treatment of various health conditions; and
- a book on homeopathy by a Swiss group of authors.^[15] This book was based on an earlier literature review of homeopathy^[16] commissioned by the Swiss Government's evaluation program for complementary and alternative medicines. Although neither the book nor the literature review was published by the Swiss Government as a health technology assessment report^[17], the NHMRC assessment considered the 2006 literature review because it is often described as a Swiss Government publication.^[18]

Figure 1. Components of NHMRC's assessment of homeopathy



How did NHMRC assess the evidence about homeopathy?

NHMRC used standardised, accepted methods for assessing the quality and reliability of evidence for whether or not a therapy is effective for treating health conditions (see NHMRC's approach to assessing health evidence).

Overview of systematic reviews

In assessing the systematic reviews, the following factors were considered:

- the relevance of the review to the question of whether or not homeopathy is effective for treating health conditions;
- the type of studies and whether they were well designed;
- whether the reports included enough information to judge whether the studies were done well and whether the results were likely to be reliable or unreliable;
- whether studies included enough participants to provide meaningful results; and
- whether studies compared homeopathy with placebo or with another treatment.

The overview considered only studies with these features:

- the health outcomes to be measured were defined in advance; the way to measure the effects of treatment on these outcomes was planned in advance; and the results were then measured at specified times (prospectively designed studies); and
- the study compared a group of people who were given homeopathic treatment with a similar group of people who were not given homeopathic treatment (controlled studies).

For each health condition, all the available evidence was grouped together to form a body of evidence on that condition. A body of evidence was considered more reliable if it included studies that were high quality, well designed and with enough participants to make its results meaningful. A body of evidence was considered less reliable if there were very few studies, or if the studies were poor quality, badly designed, or included too few participants. The methods are described in detail in the Overview Report.^[2]

For each health condition, the body of evidence was summarised in a statement, using standard wording and applying the same considerations consistently (see Appendix C).

In general, the systematic reviews included in the overview did not consider or evaluate the potential for publication bias (see Limitations of the assessment and evidence base for homeopathy). Therefore, it was not possible to estimate whether the results of unpublished studies may have altered the balance of evidence.

Evidence provided by homeopathy interest groups and individuals

The preliminary and public consultation submitted literature was assessed using a similar method to that applied in the overview. Only prospectively designed and controlled studies conducted in humans (including randomised controlled trials, pseudo-randomised controlled trials, non-randomised controlled trials and prospective cohort studies) were considered.

NHMRC did not consider observational studies, individual experiences and testimonials, case series and reports, or research that was not done using standard methods.

Studies that had already been identified and included in the overview were not considered again. For the remaining prospectively designed and controlled studies that had not already been included

in the overview, the quality of each study was evaluated using a standardised, internationally accepted method.

A full description of the methods used are provided in the *Effectiveness of homeopathy for any clinical condition: evaluation of the evidence—Review of submitted literature*^[3] and *Effectiveness of homeopathy for clinical conditions: evaluation of the evidence—Review of literature from public submissions*.^[4]

For more information on NHMRC's processes for reviewing evidence, see About the NHMRC assessment of the evidence.

What quality checks were applied to NHMRC's assessment of the evidence on homeopathy?

NHMRC has a number of processes in place to ensure that the evidence was identified and reviewed in a robust and transparent manner. In developing this Information Paper, the following steps occurred:

- expert, methodological review of the research methods used to identify and analyse the evidence in the overview report;
- the opportunity for the public to comment on the clarity of the draft Information Paper as well as submit additional evidence for consideration, through a public consultation process;
- expert review of the draft Information Paper to ensure that evidence had been interpreted in an appropriate, robust and transparent manner; and
- consideration of the Information Paper and supporting documents by the Council of NHMRC. Recommendation to release the advice is provided by Council when it is satisfied that the process followed is robust and transparent.

Expert review

NHMRC commissioned an independent organisation with expertise in research methodology (The Australasian Cochrane Centre) to review the methods used in the overview and ensure that processes for identifying and assessing the evidence were scientifically rigorous, consistently applied, and clearly documented. All the reviewer's comments and suggestions were considered in consultation with the Homeopathy Working Committee and the report amended accordingly.

NHMRC invited three national and international reviewers, with expertise in complementary medicines research, to comment on the draft Information Paper to ensure that the evidence had been accurately interpreted. All comments received were considered by the Homeopathy Working Committee and the draft Information Paper was amended accordingly. A summary of the expert reviewers' comments and the considerations of the Homeopathy Working Committee is available at www.nhmrc.gov.au/guidelines-publications/cam02.

Public consultation

A public consultation process was undertaken on the draft Information Paper. Public consultation ensured that relevant studies, examining the effectiveness of homeopathy that occurred outside of the search dates of the systematic reviews included in the overview, could be considered. Consultation also provided the opportunity for comment on the clarity of the process by which the Homeopathy Working Committee translated the research findings into advice.

All comments received from public consultation were collated and considered by the Homeopathy Working Committee. A report outlining the common themes raised during public consultation, the Homeopathy Working Committee consideration of those themes and the subsequent changes to the Information Paper is available at www.nhmrc.gov.au/guidelines-publications/cam02.

Findings of the NHMRC assessment of the evidence

Overview

The overview^[2] considered 57 systematic reviews that assessed the effectiveness of homeopathy (individualised homeopathy or clinical homeopathy) compared to placebo or other treatment, for treating health conditions.

These systematic reviews searched for published research on homeopathy for 68 health conditions and found published research on 61 of these conditions. No published research was found for the remaining seven conditions.

The systematic reviews included 176 individual studies. The overview assessed the quality and considered the findings of each study using the information provided in the systematic reviews. A list of all included studies is available at www.nhmrc.gov.au/guidelines-publications/cam02.

Based on all the evidence considered, there were no health conditions for which there was reliable evidence that homeopathy was effective. No good-quality, well-designed studies with enough participants for a meaningful result reported either that homeopathy caused greater health improvements than placebo, or caused health improvements equal to those of another treatment.

Homeopathy compared with placebo

Studies that compare a medicine with placebo are designed to test whether the medicine is effective as a treatment for the health condition. The systematic reviews identified studies that compared homeopathy with placebo for 55 health conditions (this included one condition, diarrhoea in children, for which studies of a combined homeopathy tablet (clinical homeopathy) and studies of individualised homeopathy were analysed separately).

For 13 health conditions (Table 1), homeopathy was reported to be not more effective than placebo in either:

- all the studies found (regardless of size and quality), or
- a large majority of those studies that were reliable (good-quality, well designed and with enough participants for a meaningful result).

For 14 health conditions (Table 1), some studies reported that homeopathy was more effective than placebo, but these studies were not reliable. They were not good quality (well designed and well done), or they had too few participants, or both. To be confident that the reported health benefits were not just due to chance or the placebo effect, they would need to be confirmed by other well-designed studies with adequate numbers of participants.

For 29 health conditions (Table 1), only one study that compared homeopathy with placebo was found and each of these studies was unreliable. They were either poor quality (poorly designed or poorly done) or unknown quality, or they had too few participants, or both. For these conditions, it was not possible to make any conclusion about whether homeopathy was effective or not.

Homeopathy compared with other treatments

Studies that compare a medicine with another treatment are designed to test whether the medicine is as effective as, or more effective than, existing treatment options. This type of study is normally used when previous studies have already shown that the test medicine is more effective than placebo. The systematic reviews identified studies that compared homeopathy with at least one other treatment for 15 conditions (these included 10 health conditions for which there were also studies that compared homeopathy with placebo).

Comparative studies can only provide useful information if the comparator treatment is already known to be effective. Some studies that compare two treatments also include a group of people who receive placebo, to make sure health effects in the groups taking the test medicine or the comparator treatment are not just due to the placebo effect.

In some studies considered in NHMRC's assessment, homeopathy was compared with treatments that were not standard treatments for the condition. In those studies, it was not possible to judge the true effect of homeopathy on the health condition.

For eight health conditions (Table 1), some studies reported that homeopathy was as effective as another treatment, or more effective than another treatment, but these studies were not reliable. They were not good quality (well designed and well done), or they had too few participants, or both. To be confident that the reported health benefits were not just due to chance or the placebo effect, they would need to be confirmed by other well-designed studies with adequate numbers of participants.

For seven health conditions (Table 1), only one study that compared homeopathy with another treatment was found and each of these studies was unreliable. They were either poor quality (poorly designed or poorly done) or unknown quality, or they had too few participants, or both. For these conditions, it was not possible to make any conclusion about whether homeopathy was effective or not.

These findings are reported in detail in *Effectiveness of homeopathy for any clinical condition: evaluation of the evidence. Overview report.*^[2]

Table 1. Summary of evidence from studies of homeopathy

Conclusions	Why NHMRC reached this conclusion
<p>Homeopathy is not more effective than placebo for the treatment of these health conditions:</p> <ul style="list-style-type: none"> • adenoid vegetation in children (abnormal growth of adenoid tonsils behind the nose) • asthma • anxiety or stress-related conditions • diarrhoea in children—combined homeopathy tablet (clinical homeopathy) • headache and migraine • muscle soreness (delayed onset) • labour (inducing or shortening labour) • pain due to dental work • pain due to orthopaedic surgery • postoperative ileus (abnormally slow movement of bowel after surgery) • premenstrual syndrome • upper respiratory tract infections (e.g. colds) • warts. 	<p>For each condition, homeopathy was reported to be not more effective than placebo in either:</p> <ul style="list-style-type: none"> • all the studies found (regardless of size and quality), or • a large majority of those studies that were reliable (good-quality, well designed and with enough participants for a meaningful result).
<p>There is no reliable evidence that homeopathy is more effective than placebo for the treatment of these health conditions:</p> <ul style="list-style-type: none"> • allergic rhinitis • attention deficit/hyperactivity disorder (ADHD) in children • bruising • chronic fatigue syndrome • diarrhoea in children—individualised homeopathy • fibromyalgia • hot flushes in women who have had breast cancer • human immunodeficiency virus (HIV) infection • influenza-like illness • rheumatoid arthritis • sinusitis • sleep disturbances or circadian rhythm disturbances • stomatitis (inflammation of the mouth) due to chemotherapy • ulcers. 	<p>For each condition, although some studies reported that homeopathy was more effective than placebo, these studies were not reliable. They were not good quality (well designed and well done), or they had too few participants to give a meaningful result, or both.</p>

Conclusions

Why NHMRC reached this conclusion

There is no reliable evidence on which to draw a conclusion about the effectiveness of homeopathy, compared with placebo, for the treatment of these health conditions:

- acne vulgaris
- acute otitis media (inflammation of the middle ear) in children
- acute ankle sprain
- acute trauma in orthopaedic patients
- amoebiasis and giardiasis (gastrointestinal conditions caused by parasites)
- ankylosing spondylitis
- boils and pyoderma (types of skin infections)
- Broca's aphasia in people who have had a stroke
- bronchitis
- cholera
- cough
- chronic polyarthritis
- dystocia (difficult labour)
- eczema
- heroin addiction
- knee joint haematoma (bruising)
- lower back pain
- nausea and vomiting associated with chemotherapy
- oral lichen planus
- osteoarthritis
- proctocolitis
- postoperative pain-agitation syndrome
- radiodermatitis (skin damage caused by radiotherapy) in women with breast cancer
- seborrhoeic dermatitis
- suppression of lactation after childbirth in women who elect not to breastfeed
- stroke
- traumatic brain injury (mild)
- uraemic pruritis
- vein problems due to cannulas in people receiving chemotherapy.

For each condition, only one study that compared homeopathy with placebo was found, and this study was unreliable. It was either poor quality (poorly designed or poorly done) or unknown quality, or it had too few participants to give a meaningful result, or both.

There is no reliable evidence that homeopathy is as effective as the other therapies for the treatment of these health conditions:

- acute otitis media or otitis media with effusion (inflammation of the middle ear) in children (compared with antibiotics, mucolytic medicines, secretolytic medicines, antipyretic medicines, nasal sprays, or monitoring the condition but not providing treatment ["watchful waiting"])
- allergic rhinitis (compared with antihistamines, cortisone or intranasal cromolyn sodium)
- anxiety or stress-related conditions (compared with lorazepam, diazepam or cognitive behavioural therapy)
- depression (compared with fluoxetine or diazepam)
- eczema (compared with corticosteroids, antihistamines, or other unspecified therapies)
- non-allergic rhinitis (compared with aspirin, xylometazoline or other therapies)
- osteoarthritis (compared with paracetamol or various nonsteroidal anti-inflammatory drugs)
- upper respiratory tract infection (compared with anti-inflammatory drugs, antibiotics or other therapies).

For each condition, although some studies reported that homeopathy was as effective as or more effective than another treatment, these studies were not reliable. They were not good quality (well designed and well done), or they had too few participants to give a meaningful result, or both.

Conclusions

Why NHMRC reached this conclusion

There is no reliable evidence on which to draw a conclusion about the effectiveness of homeopathy compared with other therapies for the treatment of these health conditions:

- burns (second- and third-degree)
- fibromyalgia
- irritable bowel syndrome
- malaria
- proctocolitis (inflammation of the rectum and colon)
- recurrent vulvovaginal candidiasis (yeast infection of the vagina and/or vulva, also called 'thrush')
- rheumatoid arthritis.

For each condition, only one study that compared homeopathy with another treatment was found, and this study was unreliable. It was either poor quality (poorly designed or poorly done) or unknown quality, or it had too few participants to give a meaningful result, or both.

Notes:

Systematic reviews included in the overview searched for, but did not find, studies assessing homeopathy in people with these conditions: borderline personality disorder, dementia, constipation in children, glaucoma, nocturnal enuresis (bedwetting), lower urinary tract symptoms in men, and chronic facial pain.

Systematic reviews included in the overview searched for, but did not find, studies that compared homeopathy with placebo in people with these conditions: burns (second and third degree), depression, irritable bowel syndrome, lower back pain, malaria, non-allergic rhinitis, and vulvovaginal candidiasis. For these conditions, systematic reviews found only studies that compared homeopathy with other treatments.

Information provided by homeopathy interest groups and individuals

Preliminary submitted literature

The findings from evidence submitted before the commissioned overview of evidence are summarised in the report *Effectiveness of homeopathy for any clinical condition: evaluation of the evidence. Review of submitted literature*.^[3]

A total of 343 articles were submitted to NHMRC, of which a large majority (234) were of a research or publication type not meeting the inclusion criteria. A further 79 articles had already been included or considered in the Overview Report. On considering the remaining 30 articles, studies were excluded if they: covered an intervention not meeting the inclusion criteria; were of a research type not meeting the inclusion criteria; did not report on efficacy outcomes; the study design confounded the results; or were not published in English. This resulted in nine studies examining the effectiveness of homeopathy for the treatment of eight different clinical conditions identified for further assessment.

Five of the eight conditions (otitis media, delayed-onset muscle soreness, depression, bruising, and sleep or circadian rhythm disturbances) were examined in the overview. The results of these studies were considered in relation to the body of evidence identified in the overview but did not alter the overall conclusions about the effectiveness of homeopathy because of their poor quality, poor design, poor reporting of the study design or method, or too few participants.

Three additional health conditions not included the overview were identified:

- pain after total abdominal hysterectomy;
- tracheal secretions in critically ill patients with a history of tobacco use and chronic obstructive pulmonary disease; and
- wound healing after foot surgery.

These studies were of poor quality. Problems included poor design, poor reporting of the study design or method, or too few participants. The results of these studies did not alter the overall conclusions about the effectiveness of homeopathy because of their poor quality, and because they were only selected examples of studies on those conditions.

Public consultation submitted literature

A detailed description of the evidence submitted during public consultation and the independent assessment is summarised in the report *Effectiveness of homeopathy for clinical conditions: evaluation of the evidence. Review of evidence from public submissions*.^[4]

A total of 48 submissions were received from consumers, consumer groups, health care professionals, homeopathy practitioners and homeopathy organisations. Of the 153 articles cited in these submissions, 94 were excluded because they did not meet the criteria for the NHMRC review (e.g. they did not investigate the treatment of health conditions in humans, they had already been considered in an earlier stage of the NHMRC review, or they were not published studies). The remaining 59 studies, which had not been included in the overview report, were assessed against pre-determined criteria for consideration. After this assessment, 17 more of these studies were excluded because they did not meet the criteria for the NHMRC review. Of the remaining 42 published studies, three represented a single study, resulting in a final total of 40 studies assessing the effectiveness of homeopathy for the treatment of health conditions, compared with no homeopathy or with other treatment. For each study, the risk of bias was systematically assessed using a standardised method (the Cochrane Collaboration's tool for assessing risk of bias)^[19] and analysed.

Health conditions already covered by the overview

The included studies investigated homeopathy for the treatment of 14 health conditions (16 studies) that were covered by systematic reviews included in the overview: rheumatoid arthritis, influenza-like illness, hot flushes, rhinosinusitis, ankle sprain, oral dryness, psychophysiological-onset insomnia, stress, dermatological reactions to radiotherapy, warts, osteoarthritis of the knee, chronic low back pain, upper respiratory tract infection and otitis media.

Most studies were assessed to have a moderate, moderate-to-high or high risk of bias. Many of these studies were poorly designed, poorly conducted or poorly reported. In addition, the studies had too few participants to be able to detect differences in health outcomes between the treatment groups.

The findings of these studies did not alter the overall conclusions of the NHMRC review. Although one small study with a low risk of bias favoured homeopathy for the treatment of cough in upper respiratory tract infections, this study did not have enough participants to outweigh the wider body of evidence considered in the overview, which found that homeopathy was not more effective than placebo overall (Table 1).

Health conditions not already covered by the NHMRC overview

The submissions also included published studies on 21 clinical conditions (24 studies) that were not covered by systematic reviews included in the overview:

- coffee-related insomnia;
- arsenic toxicity;
- anal fissures;
- haemorrhoids;
- pulmonary tuberculosis;
- plantar fasciitis;
- mental fatigue;
- acute febrile infections;
- varicose veins;
- vertigo;
- chronic periodontitis;
- cat allergy;
- diaper dermatitis;
- diabetic polyneuropathy;
- pain after tonsillectomy;
- essential hypertension;
- end-stage renal failure;
- subcutaneous mechanical injury in athletes;
- mucositis during stem cell therapy;
- post-rhinoplasty ecchymosis and oedema;
- malnourishment.

The majority of these studies reported results in favour of homeopathy. However, they were generally poor quality. Only one study^[20] was assessed as having a low risk of bias, and evaluated the effect of homeopathy, compared with placebo, on self-reported mental fatigue in 86 university staff and students. This study reported no difference between treatment groups, however it had too few participants to give a meaningful result.

For all other studies, the risk of bias ranged from moderate to high. Many of these studies were poorly designed, poorly conducted or poorly reported. Many of the studies had too few participants to be able to detect differences in health outcomes between the treatment groups.

The findings of studies on health conditions not already considered by the overview did not alter the overall conclusions of the NHMRC review. Although some studies reported results favouring homeopathy, none were high-quality studies judged to be at low risk of bias. In addition, these were only selected examples of studies on those health conditions.

Evidence-based guidelines and government reports

A number of evidence-based clinical practice guidelines published or funded by the United Kingdom National Institute for Health and Clinical Excellence recommend against the use of homeopathy for treating various health conditions, due to lack of evidence for its effectiveness.^[9-14]

A report by the United Kingdom House of Commons Science and Technology Committee stated that ‘the systematic reviews and meta-analyses conclusively demonstrate that homeopathic products perform no better than placebos’.^[8] This report concluded that any health benefits that people experience when they use homeopathy is solely due to the placebo effect.

A report on homeopathy research submitted to the Swiss government during its 1998–2005 complementary and alternative medicines evaluation program concluded that its findings were ‘compatible with the notion that the clinical effects of homeopathy are placebo effects’.^[21] Another, broader, literature review on homeopathy^[16], which included published and unpublished studies of various methodologies, was submitted to the Swiss government complementary and alternative medicines evaluation program. This work was not part of the Swiss government’s published health technology assessment^[17], but was later published independently by its authors as a summary article^[16] and as a book which concluded that homeopathy was a ‘valuable addition to the conventional medical landscape’.^[15] The Swiss government evaluation program resulted in a decision for health insurance to cease covering homeopathy.^[17] However, this decision was reversed after a popular vote in support of complementary and alternative medicines.^[17]

The difference between the findings of these publications was mainly due to their different methods for assessing research evidence. Both the United Kingdom report and the Swiss literature review have been criticised by those who disagree with their methods and findings on either side of the debate. The United Kingdom House of Commons Science and Technology Committee report^[8] was criticised by the British Homeopathic Association, which argued that the Committee failed to take into account certain systematic reviews and meta-analyses, and omitted or misrepresented evidence in favour of homeopathy.^[22] The Swiss literature review favourable to homeopathy^[16] was criticised by a review that argued it was ‘scientifically, logically and ethically flawed’, ‘misinterprets studies previously exposed as weak’ and ‘attempts to discredit randomised controlled trials as the gold standard of evidence’.^[18]

These reports and their methodologies were considered in assessing the evidence.

Overall findings based on the evidence

There is no reliable evidence from research in humans that homeopathy is effective for treating the range of health conditions considered.

There were no health conditions for which there was reliable evidence that homeopathy was effective.

For some health conditions, studies reported that homeopathy was not more effective than placebo.

For other health conditions, some studies reported that homeopathy was more effective than placebo, or as effective as another treatment, but those studies were not reliable. To be confident that the reported health benefits of homeopathy were not just due to chance or the placebo effect, they would need to be confirmed by other well-designed studies with an adequate number of participants.

For the remaining health conditions it was not possible to make any conclusion about whether homeopathy was effective or not, because there was not enough evidence.

Limitations of the assessment and evidence base for homeopathy

The studies of homeopathy were generally poor quality. For some health conditions, this meant that no conclusion could be made on whether or not homeopathy was effective. For other conditions, this meant that NHMRC could not be confident that the results reported by studies were reliable.

The overview was based on finding systematic reviews of homeopathy, rather than searching for all individual published studies of homeopathy. The advantage of this strategy was to make use of the large amount of work that had already been done by researchers around the world in finding and assessing studies and to provide an overarching picture of the whole body of evidence. However, there were also some disadvantages:

- As the overview only included systematic reviews, some individual studies of homeopathy may not have been considered (particularly recent studies published since the latest systematic reviews). This risk was offset by inviting homeopathy interest groups and the public to provide extra evidence at two stages of the review: before the overview and at public consultation on the draft of this Information Paper. From this process an additional 42 studies were considered as part of the assessment of the evidence. These studies did not alter the overall findings of the assessment of the evidence.
- To assess the quality of individual studies, the research group had to rely on the way that these were reported by systematic reviews. Details of study design (e.g. the outcomes measured and the length of follow up), the statistical significance of the results and the clinical importance of any reported health benefits were not always available. Also, the description of an individual study was sometimes inconsistent between systematic reviews. In these instances, the findings of the systematic review which was assessed to be of a higher quality was considered.
- It was not possible to separate the evidence for clinical homeopathy (in which the homeopath chooses one or more homeopathic medicines to treat a particular health condition) and individualised homeopathy (in which the homeopath matches all the person's symptoms to a single homeopathic medicine), because most of the systematic reviews did not analyse these separately. Most of the studies used clinical homeopathy.
- It was not possible to make conclusions about the effects of homeopathy on each of the specific health outcomes (e.g. pain, mobility) relevant to a particular health condition (e.g. arthritis), because of the large number of outcomes and the different reporting of outcomes between the different systematic reviews. Instead, outcomes were aggregated for each health condition and a single conclusion made.
- It was often difficult in studies to find the details of other treatments with which homeopathy was compared. To interpret the studies that compared homeopathy with another treatment, it is necessary to understand whether the other treatment is an effective standard treatment. This information was often not available from the systematic reviews.
- It is also likely that some studies assessing homeopathic treatments have never been published. Searching of clinical trials registries can identify unpublished studies and enable researchers to obtain and analyse the results, but cannot identify studies that have not been registered. The overview identified only 10 systematic reviews that reported having considered publication bias, and only two of these made a comprehensive, systematic search for missing studies.

One of these systematic reviews reported significant publication bias, which the authors suggested was primarily due to under-reporting of studies with statistically non-significant effects and with negative effects.^[2] Clinical trial registries (included the World Health Organisation Clinical Trials Registry, the US government's ClinicalTrials.gov and the Australian New Zealand Clinical Trials Registry) were searched but did not identify any extra studies.

Despite the above limitations, it is unlikely that a review of primary studies (rather than of systematic reviews) would have altered the findings. This is because the studies on homeopathy identified through this process were generally small and of poor quality (either poorly designed or poorly done). Due to the poor quality of the evidence base, the Homeopathy Working Committee had to apply caution when considering the results reported by studies. For some health conditions, this meant that no conclusion could be made on whether or not homeopathy was effective. For other conditions, this meant that NHMRC could not be confident that the results reported by studies were reliable.

NHMRC's interpretation of the assessment of the evidence on the effectiveness of homeopathy

Based on the overall findings of the assessment of the evidence of effectiveness of homeopathy, NHMRC has reached these conclusions:

- There is no reliable evidence that homeopathy is effective for treating health conditions.
- Homeopathy should not be used to treat health conditions that are chronic, serious, or could become serious.
- People who choose homeopathy may put their health at risk if they reject or delay treatments for which there is good evidence for safety and effectiveness.
- People who are considering whether to use homeopathy should first get advice from a registered health practitioner. Those who use homeopathy should tell their health practitioner, and should keep taking any prescribed treatments.

Definition of special terms

Body of evidence	The set of collected research evidence on a specified research question.
Complementary and alternative medicine	The range of health care practices, therapies, procedures and devices that are not currently considered to be part of conventional medicine.
Confidence (level of confidence)	A measure of the overall quality of evidence from studies for a health condition. The level of confidence in the body of evidence was recorded as 'very low' if any estimate of effect was uncertain (i.e. overall, the quality of the available information was not good enough to be able to estimate the true effect of homeopathy on that health condition). The level of confidence in the body of evidence was recorded as 'high' when further research was very unlikely to change confidence in the estimate of effect (i.e. the available evidence was high quality and the effect of homeopathy in that health condition was clear).
Controlled trial (controlled study)	A study in which the treatment being evaluated was compared with either another treatment, or placebo (a treatment or substance known to have no health benefits), in similar groups of people with the health condition.
Effectiveness (of a treatment for a health condition)	The extent to which a treatment works or not when used to treat health conditions in patients.
Evidence (medical evidence or clinical evidence)	Published findings of health research in humans using internationally accepted methods (e.g. studies that have been properly designed to assess whether or not a treatment is effective). It does not include individual experiences, testimonials or case reports, or research that was not done using standard methods.
Health condition (also clinical condition)	Any medical condition or health problem that causes a person to have symptoms or causes physical changes that can be recognised by a health professional. Health conditions include side effects of treatments such as medicines or surgery.
Homeopathy	A type of complementary and alternative medicine (See What is homeopathy?).
Placebo (in studies)	A sham treatment that is compared with the treatment being tested.
Placebo effect	An effect people experience when they believe that a treatment is effective, even if the treatment is a sham (e.g. an empty pill capsule or coloured water used in a study).
Prospective trial (prospective study)	A study that measures effects as they occur over time, beginning from an agreed time point (not by using records made in the past). The health outcomes to be measured are defined in advance, the way to measure the effects of treatment on these outcomes is planned in advance, and the results are then measured at specified times.

Randomised controlled trial

A study conducted in a standardised way to test whether a treatment is effective or not, by comparing it with another treatment or with placebo. This involves randomly allocating participants to receive the treatment or not, and measuring the effects on their health using pre-defined measurements.

Registered Health Practitioner

A Registered Health Practitioner, as defined in the Health Practitioner Regulation National Law, as in force in each State and Territory. For further information, please see www.ahpra.gov.au.

Statistically significant

Describes the difference between results for groups being compared in a study (e.g. a health measure in participants taking one treatment versus another treatment), when analysis of the results using standardised statistical methods has found that there is a less than one-in-20 probability that the difference is just due to chance. In a health study, 'statistically significant' results favouring one treatment or another do not mean that the finding is important for a person's overall health or is useful for making health decisions.

Study (research study)

A planned, structured scientific research project designed to see whether a treatment is effective in humans (e.g. a clinical trial).

Systematic review

A type of research that involves searching for all the published evidence (e.g. studies) to answer a particular question, such as whether a particular treatment is more effective than no treatment or as effective as another treatment for treating a specified health condition in a certain group of patients (e.g. children, adults). There are internationally accepted standards for good quality systematic reviews.

Appendix A. NHMRC evidence hierarchy, including explanatory notes

NHMRC levels of evidence for evaluating interventions (NHMRC 2009)

Level	Research question: intervention ¹
I ²	A systematic review of level II studies
II	A randomised controlled trial
III-1	A pseudo-randomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: <ul style="list-style-type: none"> • Non-randomised, experimental trial • Cohort study • Case-control study • Interrupted time series with a control group
III-3	A comparative study without concurrent controls: <ul style="list-style-type: none"> • Historical control study • Two or more single arm study • Interrupted time series without a parallel control group
IV	Case series with either post-test or pre-test/post-test outcomes

Explanatory notes

1. Definitions of these study designs are provided on pages 7–8 of *How to use the evidence: assessment and application of scientific evidence* (NHMRC 2000).
2. A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence. Systematic reviews of level II evidence provide more data than the individual studies and any meta-analyses will increase the precision of the overall results, reducing the likelihood that the results are affected by chance. Systematic reviews of lower level evidence present results of likely poor internal validity and thus are rated on the likelihood that the results have been affected by bias, rather than whether the systematic review itself is of good quality. Systematic review quality should be assessed separately. A systematic review should consist of at least two studies. In systematic reviews that include different study designs, the overall level of evidence should relate to each individual outcome/result, as different studies (and study designs) might contribute to each different outcome.

Appendix B. The Homeopathy Working Committee

The Homeopathy Working Committee was made up of experts in evidence-based medicine, study design, and complementary medicines research. The Committee's roles were:

- to guide an independent review of the evidence on the effectiveness of homeopathy. This included providing advice on methods of evaluating and interpreting relevant information.
- to guide NHMRC to produce a document that summarises current evidence on whether homeopathy is effective for health conditions, and give Australians information to help them make decisions about using homeopathy as part of their health care.

Homeopathy Working Committee members are listed in Table 2. Information about individual committee members' credentials and declarations of interest are available at www.nhmrc.gov.au/your-health/complementary-medicines/membership-homeopathy-working-committee.

Table 2. The Homeopathy Working Committee

Name and qualifications	Job title and other relevant roles
Chair Professor Paul Glasziou, MBBS, PhD, FRACGP	General practitioner Professor and Director of the Centre for Research into EvidenceBased Practice, Bond University, Queensland Expert in evidence-based medicine
Professor Peter Brooks, AM, MBBS, MD (Lund), FRACP, FAFRM, FAFPHM, MDHonCausa, FRCP (Glas, Edin)	Rheumatologist Director of the Australian Health Workforce Institute, University of Melbourne, Victoria (to September 2013) Executive Director Research, Northern Hospital, Epping, Victoria Former board member, Australian Centre for Complementary Medicine Education and Research, University of Queensland
Professor Frederick Mendelsohn, AO, MB BS, PhD, MD, FRACP	Neuroscientist Former Chair in Medicine and Director of the Howard Florey Institute, University of Melbourne, Victoria
Mr John Stubbs, BA, DipAcct	Consumer Executive Officer, canSpeak Honorary Associate, School of Medicine, University of Sydney, New South Wales Member, Australian Health Ethics Committee, NHMRC Member, Consumer Consultative Group, NHMRC

Name and qualifications	Job title and other relevant roles
Associate Professor Evelin Tiralongo, BPharm(Hons), PhD, GradCertHigherEd	Pharmacist Discipline head for complementary medicine teaching and research, School of Pharmacy and Griffith Health Institute, Griffith University, Gold Coast, Queensland Member, Clinical Trials Coordinating Centre, Griffith University Member, Society for Medicinal Plant and Natural Product Research
Dr Nikolajs Zeps, BSc(Hons), PhD	Research scientist Director, St John of God Subiaco Hospital Research network Adjunct Professor School of Health Sciences, Curtin University Adjunct Professor, Centre for Comparative Genomics, Murdoch University Adjunct Associate Professor, School of Surgery and School of Pathology and Laboratory Medicine, University of Western Australia Adjunct Associate Professor, Faculty of Medicine, University of Notre Dame, Western Australia Founding Director, Australian Clinical Trials Alliance Member, Research Committee, NHMRC Member, Australian Health Ethics Committee, NHMRC: Triennium 2010–2012
Professor Chris Baggoley, AO, BVSc(Hons), MBBS, BSocAdmin, FACEM, FIFEM Member May 2012–March 2013 Observer March–June 2013	Australian Government Chief Medical Officer

Appendix C. Criteria for the development of evidence statements

Purpose and role of the criteria

The Effectiveness of Homeopathy for Clinical Conditions: Evaluation of the Evidence—Overview Report (the Overview Report) included an evidence statement for each of the clinical conditions considered. The purpose of the evidence statement was to synthesise the type, quality and conclusions of the examined evidence base.

In order to ensure that the content and formulation of the evidence statements was consistent and transparent across each of the clinical conditions considered, the HWC agreed that it was necessary to develop a set of criteria. These criteria reflect the discussions and agreement of the HWC members about the key features of the evidence base¹. The nature of these criteria, and indeed the need for them at all, reflects many of the features of the homeopathy Overview Report, particularly:

- it was very broad in nature, including 61 clinical conditions;
- data on individual studies was limited by the information reported in the included systematic reviews and the quality, reliability and currency of those systematic reviews; and
- the overall shortcomings of the primary evidence base which was largely comprised of small studies that were not of high quality.

Introduction to the criteria

A standard format for evidence statements was developed, comprising three elements:

- Element 1: Body of evidence**
A description of the body of evidence which included the number of systematic reviews and included studies, the quality of these, the total number of participants, and a statement of findings.
- Element 2: Level of confidence**
A level of confidence (LOC) rating for the body of evidence as a whole.
- Element 3: Conclusion**
A concluding statement that described the effectiveness of homeopathy as a treatment for a particular condition, compared with either placebo or other treatment(s).

The three elements of the evidence statement were designed to be read together, to give an overall impression of the body of evidence.

¹ These criteria should not be treated as universal rules or principles that are applicable to all clinical contexts. The criteria were developed in response to a specific activity—NHMRC's overview of the effectiveness of homeopathy for treating clinical conditions in humans.

When there was a body of evidence addressing the intervention versus placebo, and another body of evidence addressing the intervention versus another comparator, two separate evidence statements were generally prepared (with all ‘other comparators’ included in the one evidence statement).

Separate evidence statements were not developed where there was more than one specific type of homeopathic intervention. For example, where one study examined ‘X’ homeopathic treatment and another examined ‘Y’ homeopathic treatment, the evidence statement refers broadly to ‘homeopathy’ rather than the specific treatment. This approach is consistent with other studies that assess the efficacy of an entire class of therapies: for example under the headings ‘antibiotics’ or ‘physiotherapy’ for some conditions.

Guidance for Element 1—Describing the body of evidence

The description of the body of evidence included

1. A statement of the **number of systematic reviews** and the **quality** of those reviews.
 - The quality of systematic reviews was assessed using the AMSTAR instrument. For the homeopathy overview, a score of 5 or less was considered poor, 6–8 medium, and 9+ good (out of a total score of either 10 or 11).
2. The number of studies included within systematic reviews, stratified by the type of those studies if relevant (RCTs or prospectively designed, non-randomised controlled studies).
 - Where relevant, the different levels of evidence were separately described, for example Level II evidence was described first, followed by Level III-1 and then Level III-2 evidence.
3. The quality of studies included within systematic reviews.
 - The quality of studies was an interpretation of the quality ratings assigned to individual studies in the systematic review/s by the authors of each review. The systematic reviews used a range of systems to assess the methodological quality of the included studies. For the homeopathy overview, studies were categorised as poor, medium or good quality based on the following:
 - Jadad scores: 1 or 2 = poor; 3 or 4 = medium; 5 = good.
 - SIGN scores: a negative (-) sign = poor; a positive (+) sign = good.
 - Internal validity scores: 0-2.5 = poor; 3-4.5 = medium; 5-6 = good.
 - Scores out of 100 and scores expressed as percentages: 0-40 = poor; 40-70 = medium; >70 = good.
 - Risk of bias assessments: ‘low’ risk of bias = good; ‘high’ risk of bias = poor; ‘unclear’ risk of bias = quality unclear.
 - Scores ‘expressed as Jadad / internal validity score’ (used in Linde et al (1997), where two separate quality scores are shown as percentages of the total maximum score (i.e. out of 100), separated by a ‘ / ’ : The first score (Jadad score expressed out of 100) was used to assess the quality of the primary studies as it was the most commonly used scoring system throughout the overview. This means that where the first score was 20 or 40 = poor; 60 or 80 = medium; 100 = good.
 - If several systematic reviews reported different quality levels for the same study there were two ways that the decision was made:
 - if more than two reviews reported a quality score, the quality reported by the majority was used for the purpose of formulating evidence statements.
 - if only two reviews reported quality scores and they were conflicting, the quality score from the review with the highest AMSTAR score was used for the purpose of formulating evidence

statements. If the reviews still could not be split, the lower quality score was used in the evidence statement to avoid any overestimation of the study's quality.

- If the quality of studies was variable, the quality range was stated, for example 'poor—medium'; 'poor—good'.
- If the authors did not assess quality then it was stated as 'unreported'.

4. The number of participants (total number of participants across all studies and the range).

- Number of participants was listed as the total number of participants ever randomised for each question, and a range for the smallest to largest study.
- Where there were only two included studies, the number of participants for each study was stated, rather than the total number of participants or the range.
- Where there was only one study, the description of the body of evidence included the size of the study described in words, as follows²:
 - < 50 : very small
 - 50 to 149: small
 - 150 to 499: medium
 - 500 to 999: large
 - ≥1000: very large

5. A description of the intervention.

- Where all studies examined one specific homeopathic treatment (eg homeopathic Arnica), this was explicitly stated. Otherwise, the intervention was simply described as 'homeopathy'.

6. A description of the comparator.

- As noted above, placebo and 'other' comparators were addressed separately, in two distinct evidence statements.
- Where multiple 'other comparators' were examined, these were referred to as 'other therapies', with details provided in brackets.
- Where only one or two other comparators were examined, the comparator was explicitly described, rather than using the term 'other therapy'.

7. A statement about the findings of the included studies / reviews.

- A description of the findings of the included studies / reviews was only included in the evidence statement where there were good quality studies of sufficient size, for example: 'The one medium sized, good quality trial ([number] participants) did not detect a difference between homeopathy and placebo in the treatment of people with [condition].'
 - For the purposes of the homeopathy overview, studies were considered to be of sufficient size where $N > 150$ (i.e. those studies categorised as 'medium' sized or larger), as the outcomes were generally continuous outcomes.
 - If different systematic reviews reported different numbers of participants for the same study, it was generally assumed that the study was of the smallest size reported to avoid any overestimation of the sample size.
 - If the study quality was unreported, it was generally assumed to be poor quality to avoid any overestimation of the study's quality.

2 Thresholds for descriptions of study sizes were determined as a general guide for intervention studies of this nature, based on the (generally) continuous outcomes measured in the studies. The following study was considered in the development of these thresholds: Influence of trial sample size on treatment effect estimates: meta-epidemiological study. *BMJ*2013;346:f2304.

- If different systematic reviews reported different quality scores for the same study, it was generally assumed that the study was of the lowest quality reported to avoid any overestimation of the study's quality.
- In theory, the results of meta-analyses may have also been discussed in this part of the evidence statement. However, it was considered that all of the meta-analyses for specific conditions (i.e. those that had the potential to be included in evidence statements) had included studies that were of poor methodological quality/had a high risk of bias. A decision was made to state the findings of studies that were of good methodological quality and sufficient size in favour of meta-analyses that included poor quality studies.
- If there was more than one study that suggested that homeopathy is more effective than placebo or as effective as other therapies but due to the number, size and/or quality of those studies the findings are not reliable, a general statement to that effect was made, for example: 'These studies are of insufficient [quality] / [size] / [quality and size] / [quality and/or size] / [quality or size] to warrant further consideration of their findings.'
- In all other circumstances, no 'statement of findings' was included in the evidence statement.
- Where a systematic review did not identify any studies, this was stated and the date of the systematic review was included, for example: 'One systematic review ([year]) did not identify any prospectively designed and controlled studies that assessed the effectiveness of homeopathy in people with [condition].'

Guidance for Element 2—Assigning a level of confidence

A level of confidence (LOC) rating was assigned to the body of evidence as a whole, for each condition.

Assigning a LOC was based on judgment and expertise using a framework informed by the GRADE framework³. Usually GRADE is applied outcome by outcome rather than to the body of evidence as a whole. This is because the availability and quality of evidence may differ for each outcome. However, an adapted version of GRADE was used in order to make broad statements about the LOC in the body of evidence as a whole.

As per the GRADE methodology, each condition's evidence base was assigned a starting LOC of 'high' (Table B.i)

Table B.i: Level of confidence (adapted from GRADE)

GRADE rating (Level of confidence: LOC)	GRADE description
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

3 For further information on the GRADE methodology see: *Grading Quality of Evidence and Strength of Recommendations*. Grade Working Group. BMJ V328, 19 June 2004.

The LOC was then upgraded or downgraded depending on the limitations or strengths of the studies contained in the systematic reviews (see Table B.ii).

Table B.ii: Upgrading and downgrading

Decrease grade if:	Increase grade if:
Serious (– 1) or very serious (– 2) limitation to study quality	Strong evidence of association—significant relative risk of > 2 (< 0.5) based on consistent evidence from two or more observational studies, with no plausible confounders (+1)
Important inconsistency (– 1)	Very strong evidence of association—significant relative risk of > 5 (< 0.2) based on direct evidence with no major threats to validity (+2)
Some (– 1) or major (– 2) uncertainty about directness	Evidence of a dose response gradient (+1)
Imprecise or sparse data (– 1)	All plausible confounders would have reduced the effect (+1)
High probability of reporting bias (– 1)	

For the homeopathy overview, the information available for downgrading evidence was predominantly as follows:

- **Quality:** -1 or -2 depending on seriousness of limitation to study quality.
 - If quality of the included studies was not reported in the systematic review then those studies were assumed to be poor quality (-2).
 - NB: if quality is assessed using Jadad then any score <5 could indicate serious or very serious bias. Therefore it was often appropriate to give a range for the LOC (i.e. subtracting both -1 and -2) e.g. moderate-low.
- **Precision:** related to the number of participants in individual studies and as a whole. Small is relative but in general any study with less than 150 participants is small.
 - Very sparse data = ≤50 (-2).
 - Sparse data = 51 – 149 (-1).
 - A level of judgement was required. For example, three small / very small studies with a total sample size of 110 might be considered ‘sparse’ to ‘very sparse’, so would be downgraded by 1–2 and a range presented.

The remaining GRADE factors were difficult to apply to an overview; however, downgrading based on the quality of the systematic review/s was also appropriate in some situations (as a poorer quality systematic review is more likely to result in bias).

Guidance for Element 3—Final conclusion

The final statement provides a conclusion (defined by the Oxford Dictionary as ‘a judgement or decision reached by reasoning’) about the effectiveness of homeopathy as a treatment for a particular condition, compared with either placebo or other treatment(s).

The conclusions were generally based on whether or not any statistically significant findings were reported for any outcome (unless it was determined that the outcome had no clinical relevance). It is acknowledge that the assessment of ‘effectiveness’ based on statistical significance and not clinical significance is not ideal. However, this approach was necessary due to the poor reporting (e.g. no reporting of primary outcomes, effect estimates or confidence intervals) and lack of analyses by the included systematic reviews and primary studies. Further, it was not possible to create a hierarchy of clinically relevant outcomes prior to conducting the overview (due to the number of conditions and systematic reviews included in the overview) and making post hoc decisions about the importance of outcomes is likely to be subject to bias.

There are two approaches for designing studies to evaluate medicines; null hypothesis and estimation of effect. The standard approach used in Health Technology Assessments is the null hypothesis, with the onus of proof on those who are proposing that the treatment be used (e.g. manufacturers, practitioners or researchers). Any claims about the effectiveness of a medicine are not accepted without evidence from clinical trials that compare the treatment with placebo in patients with the clinical condition.

In this review of homeopathy, the null hypothesis for each clinical condition was that homeopathy has no effect as a treatment for that condition unless there was sufficient reliable evidence to demonstrate otherwise. The only exceptions to this principle were:

- where there were no studies (or only one small and/or poor/unknown quality study) identified for a particular clinical condition; or
- where the evidence was so poorly reported so as to be uninterpretable.

In these cases, the HWC determined that no conclusion could be drawn about effectiveness, rather than assuming the null hypothesis.

In general, separate conclusions were not developed where there was more than one specific type of homeopathic intervention. That is, where one study examined 'X' homeopathic treatment and another examined 'Y' homeopathic treatment, the conclusion refers broadly to 'homeopathy' rather than the specific treatment. The only exception to this principle was for the condition 'Children with diarrhoea', where there was a difference in the evidence base for 'combined homeopathy' and 'individualised homeopathy'. In this instance, the conclusion sentence separately reflected the evidence base for each type of homeopathy.

In the final concluding statement, the intervention is described as 'homeopathy' even if a more detailed description is provided in Element 1 of the evidence statement.

For studies that compared homeopathy with placebo, the null hypothesis assumed by the HWC was that homeopathy is no more effective than placebo.

For studies that compare homeopathy with another therapy, the null hypothesis assumed by the HWC was that homeopathy is not as effective as the other therapy. It is noted however, that due to the scope of the homeopathy overview, the *appropriateness* of the comparator was generally not assessed. For the purpose of framing the null hypothesis, an implicit assumption has been made that the comparator is more effective than placebo (i.e. the concluding statement is based around whether homeopathy is 'as effective as' another treatment, without a consideration of the appropriateness of that treatment). The HWC acknowledged that this could mean that homeopathy is found to be 'as effective as' an ineffective treatment.

Further detail on the development of evidence statements is provided at Appendix C of the Overview Report.^[2]

References

1. National Health and Medical Research Council, *NHMRC Strategic Plan 2013–2015* 2012, Canberra: NHMRC.
2. Optum, *Effectiveness of homeopathy for any clinical condition: evaluation of the evidence. Overview report* 2013, Canberra: NHMRC.
3. Optum, *Effectiveness of homeopathy for any clinical condition: evaluation of the evidence. Review of submitted literature* 2013, Canberra: NHMRC.
4. Australian Research Centre for Health of Women and Babies, *Effectiveness of homeopathy for clinical conditions: evaluation of the evidence. Review of evidence from public submissions* 2014.
5. World Health Organization, *Safety issues in the preparation of homeopathic medicines* 2009, Geneva: WHO.
6. National Health and Medical Research Council, *How to review the evidence: systematic identification and review of scientific literature* 1999, Canberra: NHMRC.
7. *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines* 2009: NHMRC.
8. House of Commons Science and Technology Committee, *Evidence check 2: Homeopathy* 2010, London: The Stationery Office.
9. National Institute for Health and Clinical Excellence, *Caesarean section. NICE clinical guideline 132 [Last modified August 2012]* 2011, London: NICE.
10. National Institute for Health and Clinical Excellence, *Neonatal jaundice. NICE clinical guideline 98* 2010, London: NICE.
11. National Institute for Health and Clinical Excellence, *Surgical management of otitis media with effusion in children. NICE clinical guideline 60* 2008, London: NICE.
12. National Collaborating Centre for Women’s and Children’s Health, *Induction of labour* 2008, London: RCOG Press.
13. Royal College of Physicians, *The management of lower urinary tract symptoms in men. NICE Clinical Guidelines No. 97* 2010, London: National Clinical Guideline Centre, The Royal College of Physicians.
14. National Collaborating Centre for Women’s and Children’s Health, *Atopic eczema in children. Management of atopic eczema in children from birth up to the age of 12 years* 2007, London: RCOG Press.
15. Bornhöft, G. and P. Matthiessen, eds. *Homeopathy in healthcare—Effectiveness, appropriateness, safety, costs*. 2012, Springer: Berlin.
16. Bornhoft, G., et al., *Effectiveness, safety and cost-effectiveness of homeopathy in general practice—summarized health technology assessment*. *Forschende Komplementarmedizin* (2006), 2006. 13 Suppl 2: p. 19–29.
17. Gurtner, F., *The report “Homeopathy in healthcare: effectiveness, appropriateness, safety, costs” is not a “Swiss report”*. *Swiss Medical Weekly*, 2012. 142: p. w13595.
18. Shaw, D.M., *The Swiss report on homeopathy: a case study of research misconduct*. *Swiss Medical Weekly*, 2012. 142: p. w13594.

19. Higgins, J.P.T. and S. Green, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]*. 2011, The Cochrane Collaboration.
20. Dean, M.E., et al., *Homeopathy for mental fatigue: lessons from a randomized, triple blind, placebo-controlled cross-over clinical trial*. BMC complementary and alternative medicine, 2012. 12: p. 167.
21. Shang, A., et al., *Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy*. Lancet, 2005. 366 (9487): p. 726–32.
22. British Homeopathic Association, *The Science & Technology Select Committee Evidence Check on Homeopathy: British Homeopathic Association response to report 2010*: British Homeopathic Association.