Homeopathy for depression: a systematic review of the research evidence.

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This is an electronic version of an article published in Homeopathy, 94 (3), pp. 153-163, July 2005. The definitive version in Homeopathy is available online at:

http://www.sciencedirect.com/science/journal/14754916

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Homeopathy for depression: a systematic review of the research evidence

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**Short running title:** Systematic review of homeopathy in depression

**Keywords:** homeopathy, depression, depressive disorder, systematic review
Abstract

Objective
To systematically review the research evidence on the effectiveness of homeopathy for the treatment of depression and depressive disorders

Methods
A comprehensive search of major biomedical databases including MEDLINE, EMBASE, CINAHL, PsycINFO and the Cochrane Library was conducted. Specialist complementary and alternative medicine (CAM) databases including AMED, CISCOM and Hom-Inform were also searched. Additionally, efforts were made to identify unpublished and ongoing research using relevant sources and experts in the field. Relevant research was categorised by study type and appraised according to study design. Clinical commentaries were obtained for studies reporting clinical outcomes.

Results
Only two randomised controlled trials (RCTs) were identified. One of these, a feasibility study, demonstrated problems with recruitment of patients in primary care. Several uncontrolled and observational studies have reported positive results including high levels of patient satisfaction but because of the lack of a control group, it is difficult to assess the extent to which any response is due to specific effects of homeopathy. Single case reports/studies were the most frequently encountered clinical study type. We also found surveys, but no relevant qualitative research studies were located.
Adverse effects reported appear limited to ‘remedy reactions’ (‘aggravations’) including temporary worsening of symptoms, symptom shifts and reappearance of old symptoms. These remedy reactions were generally transient but in one study, aggravation of symptoms caused withdrawal of the treatment in one patient.

Conclusions

A comprehensive search for published and unpublished studies has demonstrated that the evidence for the effectiveness of homeopathy in depression is limited due to lack of clinical trials of high quality. Further research is required, and should include well-designed controlled studies with sufficient numbers of participants. Qualitative studies aimed at overcoming recruitment and other problems should precede further RCTs. Methodological options include the incorporation of preference arms or uncontrolled observational studies. The highly individualised nature of much homeopathic treatment and the specificity of response may require innovative methods of analysis of individual treatment response.

Keywords: homeopathy, depression, depressive disorder, systematic review
Introduction

Mental health problems such as anxiety, depression and insomnia are among the most common reasons for individuals to seek treatment with complementary therapies in the US.¹ This survey revealed that prevalence of the use of complementary and alternative medicine for the United States in 1997 was 42 per cent with chronic conditions, including depression and anxiety, comprising the conditions for which therapies were most frequently sought: 40.9% of adults with depression and 42.7% of adults with anxiety had used complementary therapies in the previous year.¹

Several surveys have focussed on the use of complementary and alternative medicine by patients with psychiatric disorders. Davidson and colleagues conducted a study to determine the frequency of psychiatric disorders in patients receiving complementary medical care in the UK and the USA.² Psychiatric disorders were relatively frequent among these patients. 74% of the British patients and 60.6% of the American patients had a lifetime psychiatric diagnosis. Major depression (52% of UK patients and 33.3% of USA patients) and any anxiety disorders were the commonest lifetime diagnoses. 46% of the UK patients and 30.3% of the USA patients had a current psychiatric diagnosis. Six per cent of the total currently suffered from a major depression and 25.3% of the total met the criteria for at least one anxiety disorder. A high rate of use of complementary therapies in adults who met criteria for common psychiatric disorders was also reported by Unutzer and colleagues.³ Respondents who met the criteria for major depression and panic disorder were particularly likely to report use. Finally, a recent, large, prospective
study of 3981 patients consulting classical homeopaths in Germany demonstrated a similar situation with depression among the 10 most frequent diagnoses encountered.\(^4\)

**Depression**

Depression refers to a wide range of mental health problems characterised by the absence of a positive affect, low mood and a range of associated emotional, cognitive, physical and behavioural symptoms. Behavioural and physical symptoms typically include tearfulness, irritability, social withdrawal, reduced sleep, exacerbation of pre-existing pain and pain secondary to increased muscle tension and other causes, poor appetite, lack of libido, fatigue and diminished activity, although agitation is also common and marked anxiety frequent. Along with a loss of interest and enjoyment in everyday life, feelings of guilt, worthlessness and deserved punishment are common, as are lowered self-esteem, loss of confidence, feelings of helplessness, suicidal ideation and attempts at self-harm or suicide. Cognitive changes include poor concentration and reduced attention, pessimistic and recurrently negative thoughts about oneself, one’s past and the future, mental slowing and rumination.

Depression is the most common mental disorder in community settings, and is a major cause of disability across the world. In 1990, it was the fourth commonest cause of loss of disability adjusted life years in the world, and by 2020, it is projected to become the second commonest cause.\(^5\) The estimated point prevalence for major depression among 16 to 65 year olds in the UK is 21/1000. If the broader category of "mixed depression and anxiety" is included, this rises to 98/1000. Apart from the subjective suffering
experienced by people who are depressed, the impact on social and occupational
functioning, physical health and mortality is substantial. The impact on physical health
sets depression alongside all the major chronic and disabling physical illnesses such as
diabetes, arthritis and hypertension.6

A range of therapeutic approaches are available, the most widely used, in developed
countries, is antidepressant drugs.7 However these are associated with a number of
problems including poor compliance and toxicity in overdose (particularly with the older
tricyclic drugs) while the more modern selective serotonin uptake reinhibitor (SSRI)
drugs are associated with increased incidence of self harm in young people and of suicide
8,9. Patients may turn to complementary therapies due to side effects of medication, time
and effort associated with non-pharmacological therapies, lack of response or simply
preference for the complementary approach.

**Homeopathy**

Homeopathy is among the most popular of CAM therapies and is widely used in western
European countries including France, Germany, the Netherlands and the UK. It is also
popular elsewhere in the world, notably the Indian subcontinent and Latin America and
there has been rapid recent growth of usage in the USA1. Its perceived safety is an
important factor motivating patients to use homeopathy.10 The extensive use of
homeopathy, together with interest in homeopathy as a treatment for depression11,12,13
suggested that a review of the evidence for effectiveness in this condition would be
valuable.
**Aim and objectives**

The aim of this study was to evaluate the evidence from a range of sources on the effectiveness (and safety and patient satisfaction) of homoeopathy for the treatment of depression.

**Methods**

**Summary of search strategy**

A comprehensive search for clinical research was carried out. Systematic searches were conducted on a range of databases, citations were sought from relevant reviews and several websites were also included in the search, including those of MIND and the Mental Health Foundation.

**Databases searched**

General:

CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, EMBASE, MEDLINE (and PubMed), PsycINFO, TRIP (Turning Research Into Practice) database

Specialist CAM and condition based:

Search terms

The basic search terms for homeopathy included:

Exp homeopathy or Exp homeopathic drugs or Homoeop* or Homeop*

Terms for depression included:

Exp depression or Exp depressive disorder(s) or Exp dysthymia or Exp dysthymic disorder(s) or Depress* or Dysthym* or Mood or Affective disorder(s)

Search strategies were adapted for each of the databases searched and the CCDAN register and Hom-Inform databases were searched by the information specialists responsible for these databases. Efforts were made to identify unpublished and ongoing research using relevant databases such as the National Research Register (UK) and Clinicaltrials.gov (US) together with experts in the field. Searches of databases (general and specialist) were initially conducted from inception up to October 2003 and then repeated in February 2004 and searches for unpublished studies carried out in May 2004.

Filtering

Relevant research was categorised by study type according to a flow-chart system developed for this project. The basic categories used are shown in Table 1. Animal research and basic lab-based research were not included in the categorisation process.
Selection criteria

Types of study

- Initially only controlled studies were selected (randomised and non-randomised). As very few were located, other studies such as uncontrolled and observational studies were also included. Attempts were also made to locate relevant qualitative studies.

- No language restrictions were imposed at the search and filtering stage and translations were obtained for any potentially relevant studies in languages other than English.

Types of participants

- Participants with a primary diagnosis of depression or a depressive disorder and those with depression as part of a result of a physical illness.

Interventions

- All forms of homeopathy including individualised and complex. (Homeopathic complexes are fixed combinations of several homeopathic medicine)

Outcome measures

- Depression rating scales and patient focused measures such as satisfaction where relevant.
Data collection and analysis

Data was extracted systematically using a specially designed data extraction form. Data extracted included details of selection criteria and procedure, the participants, the intervention and any comparison or control intervention, aspects of the methodology and outcome measures and results. Clinical trials were appraised using a standardised appraisal framework specifically developed for this project and based on criteria recommended in the Centre for Reviews and Dissemination Report Number 4 (2nd Edition), Undertaking Systematic Reviews of Research on Effectiveness.\textsuperscript{14}

Evaluation criteria included method of randomisation, allocation concealment and level of blinding (if relevant), method of dealing with missing values, loss to follow-up/withdrawals, measures of compliance and outcomes measures reported. The full criteria are shown in the tables of studies.

Data extraction and appraisal were conducted independently by two researchers (KP, GK) for each study and any disagreements or discrepancies were resolved by discussion. Where consensus could not be obtained, a third reviewer (JR) was available for consultation.

Clinical commentaries

Clinicians with training and experience in psychiatry and homeopathy and clinical research in these area (HR, PF) commented on studies focusing on clinical relevance and
practical issues. Commentary frameworks were specifically developed for this project, these incorporate a number of closed and open questions with space for further comments. Summaries of these commentaries are provided in the tables of studies.

**Main results**

**Types of study and numbers identified (Figure 1)**

Systematic reviews:

- No systematic reviews specifically on the topic of homeopathy for depression were identified. One systematic review\(^\text{15}\) included an RCT of patients with mixed anxiety and depression\(^\text{16}\) (included under Controlled clinical trials)

Controlled clinical trials:

- Depression as primary diagnosis
  - 2 RCTs\(^\text{16,17}\) were identified

- Depression as secondary diagnosis/part of physical illness
  - 1 RCT (depression associated with chronic fatigue syndrome)\(^\text{18,19}\) was located

Other studies located:

- 4 UCT/case series\(^\text{20,21,22,23,24}\)
- 1 observational survey-based study\(^\text{25}\)
- 1 multivariate analysis\(^\text{26}\)
• Over 50 single case reports/studies
• A number of surveys and patient outcome studies

No relevant qualitative research studies were located

Language of studies located

Only one study in a language other than English was located\textsuperscript{16}. A translation was obtained.

The Evidence

Based on conventional measures of quality and accepted study types, i.e. adequately randomised and controlled studies of sufficient power, no relevant studies were located. Those that were located were of low methodological quality, had insufficient numbers of participants or were uncontrolled. However, all located studies are presented in the tables together with comments on their methodology and clinical relevance in an attempt to highlight the issues to be addressed in future research in this area.

Summary of each study

Only one published randomised controlled trial examining the use of homeopathy for depression was located. This trial\textsuperscript{16}, conducted in France, has been described previously as an ‘open randomised study’\textsuperscript{27} comparing homeopathic treatment with diazepam in patients with mixed anxiety and depressive states. Positive results for an homeopathic complex, a standardised proprietary formula, were reported. In the criteria-based systematic review of Kleijnen and colleagues\textsuperscript{15} the trial scored only 45 out of 100 for
methodological rigour, the cut off point for better studies was ≥55. The use of an anxiolytic drug as a control appears inappropriate in a trial in patients with depression and further appraisal of the study revealed a lack of information on many of the measures of trial quality; the method of randomisation, whether assessors were blinded, compliance and co-interventions. There were also problems in the diagnostic classification and inappropriate outcome measures were used. In subsequent meta-analyses and reviews, no further controlled trials specific to homeopathy and depression are cited. 28,29,30,31,32 Studies conducted by the Homoeopathic Medicine Research Group, as a report to the European Commission, also failed to uncover any new controlled trials. 33,34

A randomised controlled trial of homeopathy for depression in primary care was, however, conducted in 1999 at an East London group practice in collaboration with the Royal London Homeopathic hospital. 17 The aim of this pilot study was to assess the feasibility of a general practice based trial comparing the effectiveness of individualised homeopathic treatment against fluoxetine (Prozac) and placebo. The methodology described is rigorous; randomised, double blind and double dummy. However, difficulties with recruitment resulted in only 11 participants being recruited to the study, 4 in the treatment group with only 5 patients completing the study (personal communication).

Davidson and colleagues reported homeopathic treatment of 12 patients with a range of diagnoses related to depression and anxiety disorders. 21 Full psychiatric diagnostic assessment together with a comprehensive homeopathic interview took place followed by
individualised prescribing of the homeopathic treatment. 7 (58%) of patients were reported to have responded to homeopathic treatment, on the basis of the Clinical Global Improvement (CGI) scale, including 2 of the 3 patients with major depression. Type and potency of the remedies, duration of treatment and co-interventions varied between patients, as did the initial diagnoses leading to difficulties in interpreting the results. However, this study was considered relevant to practice and valuable as a preliminary report by a clinical commentator involved in the current review.

There are several studies of the effects of homeopathy on mood or depression scores (among other outcomes), in patients with conditions such as cancer and chronic fatigue syndrome.

A 1 year randomised controlled trial of the treatment of 64 patients with post viral fatigue syndrome or ME (myalgic encephalomyelitis), included self-assessed mood disturbance as an outcome measure and found greater improvement in the syndrome overall with patients treated with individualised homeopathy compared with those in the placebo group. However, no other measures of mood or depression were taken and the significance of these results for patients with other conditions is unclear. For this reason, further details of this study are not included in the table of studies.

The studies in cancer patients are all uncontrolled and involve the use of homeopathy to treat a range of problems. Depression was only one of the problems reported and measured. These studies provide only relatively weak evidence of effectiveness, as lack
of a control group and reporting of a range of outcomes leads to difficulties in interpretation of the results, particularly when assessing the extent to which any response is due to treatment with homeopathy. However, the findings are relevant to practice and therefore will be described here.

Clover and colleagues reported a series of 50 cancer patients in whom response to homeopathy treatment had been assessed using the Hospital Anxiety and Depression Scale (HADS) and Rotterdam Symptom Checklist. Improvements were seen on the psychological distress subscale of the latter when comparing scores on initial and later (3rd and 4th) visits and the percentage with normal HADS anxiety scores increased from 48% to 75% over this period. However, the lack of a control group, variable co-interventions and loss to follow-up of 58% lead to difficulties in interpretation of these findings.

More recently, in a well-designed uncontrolled clinical trial of the use of individualised homeopathy for symptom relief in 100 cancer patients, 52% of patients were found to have some improvement in depression scores at the end of the study period. Up to 3 symptoms perceived by the patient as problematic were rated on a self-rating scale. Mood disturbance was assessed using the Hospital Anxiety and Depression Scale (HADS). At the beginning of the study, 37 patients were depressed with 20 having a diagnosis of depression (scores above 10) and 17 borderline depression (scores 8-10). There was a significant improvement in the mean depression score for the whole study group, comparing the baseline score with either the average over all visits or just the last visit (p<0.05). Overall, 52% of patients were found to have some improvement in depression
scores at the end of the study period (4-6 consultations later), with a mean improvement of 1.4 (95% CI 0.1-2.6). Attrition rate was high; only 52% completed the study and 17 patients suffered an aggravation of symptoms or return of old symptoms considered to be previously described remedy reactions. No adverse reactions resulted in withdrawal of treatment. Satisfaction with treatment was measured by self-completion questionnaire and was high amongst those who completed the study; 75% regarded homeopathic treatment as having been helpful or better.

In a further uncontrolled clinical trial of individualised homeopathy for symptoms of oestrogen withdrawal in 45 breast cancer patients, a significant improvement in depression score was found among women with depression, but not of the group overall. Twenty-six of the patients had also been included in the 2002 study. 89% of patients completed this study and again satisfaction with treatment was high; 67% regarded homeopathic treatment as having been helpful, very helpful or extremely helpful for their symptoms.

An observational survey-based study of homeopathic treatment in 269 women with gynaecological disorders, 38% of whom were assessed as having mood disorders has been reported. However, no information is given on diagnosis, the information was extracted from standardised questionnaires completed by 31 gynaecologists and the 269 questionnaires returned represented a response rate of only 28.5%. Response to treatment was based on physician and patient assessment rated on a 5-point scale and for 67% of
women in the study (calculated on an intention-to-treat basis) a ‘very good’ or ‘good’ improvement in their mood disorder symptoms was recorded.

Finally, outcome studies including those of Clover, Richardson and van Wassenhoven and Ives have reported positive results in patients with a range of conditions including depression.

In summary, only two randomised controlled trials were identified. One of these, a feasibility study, is published in this issue of Homeopathy. It demonstrated problems with recruitment of patients in primary care. Several uncontrolled and observational studies have reported positive results including high levels of patient satisfaction. Because of the lack of a control group, it is not possible to assess the extent to which any response is due solely to the homeopathy. The interventions also varied including various types of homeopathy: individualised prescribing, ‘limited list’ prescribing and standardised complexes, further complicating interpretation of the findings.

Adverse effects reported in the studies located appear limited to ‘aggravations’ including temporary worsening of symptoms, appearance of new symptoms and reappearance of old symptoms. These reactions were generally transient but in one study, aggravation of symptoms caused withdrawal of the treatment in one patient.
Conclusions

A comprehensive search for published and unpublished studies has demonstrated that the evidence for the effectiveness of homeopathy in depression is limited due to a lack of clinical trials of high quality. When attempted, RCTs of good design have encountered problems, particularly with recruitment. Similar problems have been encountered in other RCTs in depression. The adverse effects reported in the studies were congruent with literature on the safety of homeopathy suggesting that homeopathic medicines may provoke adverse effects but these are relatively rare, mild and transient, although there is probably under-reporting.\(^{37,38}\) A recent systematic review of the frequency of homeopathic aggravations in the placebo and verum groups of double-blind, randomised clinical trials did not identify clear evidence of the existence of homeopathic aggravations\(^{39}\) contrary to the findings of audits in practice\(^ {40}\). The situation with regard to safety can be summed up as follows:

> "Homeopathic medications in high dilutions prescribed by trained professionals are probably safe and unlikely to provoke severe adverse reactions. It is difficult to draw definite conclusions due to the low methodological quality of reports claiming possible adverse effects of homeopathic medicines." \(^ {37}\)

Implications for the future

If shown to be effective, homeopathy might be a useful therapeutic option in depression; potential benefits over existing treatments include high patient acceptability, lack of adverse effects and safety in overdose. However the evidence base is currently weak. The main problem in RCTs of homeopathy for depression has been recruitment. In
principle it is possible to overcome this problem by using a very large recruitment base. However, this would be inefficient and the low recruitment ratio such a design implies means that the recruited subjects would likely be atypical.

Further research is required, and should include well-designed controlled studies with sufficient numbers of participants. However, before launching such studies, development of methodologies and strategies to overcome recruitment problems is necessary. Patient preference, and the attitudes of health professionals appear to be important constraints to recruitment. Qualitative studies aimed at identifying and understanding patients’ and health professionals’ perceptions and attitudes should precede further RCTs. Methodological options include the incorporation of preference arms or uncontrolled observational studies although both are less rigorous than RCTs.\(^4\), when well-designed, such studies give results similar to those of randomised controlled studies.\(^5\) The highly individualised nature of much homeopathic treatment and the claimed specificity of response justifies innovative methods of analysis of individual response to treatment. For instance in ‘participant-centred analysis’, subjects are declared benefited, non-responder or harmed, on the basis of a predefined decision rule. Variables associated with these responses can then be analysed.\(^3\)

Finally, a substantial number of case studies were located. These provide an indication of the range of remedies employed in patients whose symptoms include depression. However, conclusions about the effectiveness of homeopathic treatment cannot be drawn from these because of factors such as preferential reporting of successful or unusual cases, and regression to the mean. Such reports however might provide useful qualitative data concerning homeopathic treatment strategies, but synthesis of information from
individual case reports is complex and impeded by a lack of structure and absent information in many reports. Efforts to encourage the publishing of high-quality structured case reports, or consecutive case series of may help to address these problems. Methods aimed at utilising or synthesising data held with individual case studies either as a potential form of evidence or at least, as an illustration of how homeopathy is used in individuals with depression, may prove a valuable and rewarding approach in the future.

**Summary of studies**

See separate file

**Acknowledgements**

Anelia Boshnakova, Electronic Information Officer, RCCM for advice and support with search strategies and searches.

Veronica Tuffrey, Senior Lecturer, School of Integrated Health, University of Westminster for advice and comments on statistical issues.

The Project Advisory Group and Specialist Advisory Group (mental health) for the NHS Priorities Project for advice and support to the project.
The NHS Priorities Project is funded by the Department of Health. The views and opinions expressed are those of the authors and do not necessarily reflect those of the Department of Health.

References


7 Boyer WF, Feighner JP. The financial implications of starting treatment with a selective serotonin reuptake inhibitor or tricyclic antidepressant in drug-naive depressed patients. In *Health Economics of Depression* eds Jonsson and Rosenbaum. Chichester: J Wiley 1993


Figure 1 - Types of studies and numbers identified
Table 1 – Categories of study types used

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT</td>
<td>randomised controlled trials</td>
</tr>
<tr>
<td>CCT</td>
<td>controlled clinical trials (without randomisation)</td>
</tr>
<tr>
<td>UC studies</td>
<td>uncontrolled studies including uncontrolled clinical trials and case series (further categorised according to the study population i.e. random sample, consecutive series or ‘best’ series)</td>
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<tr>
<td>Case reports/studies</td>
<td>reports of individual cases/patients</td>
</tr>
<tr>
<td>Qualitative research</td>
<td>study designs with a qualitative approach (including in-depth interviews and focus groups)</td>
</tr>
<tr>
<td>Surveys</td>
<td>large scale, primarily quantitative structured approaches</td>
</tr>
<tr>
<td>Other</td>
<td>research studies not falling into above categories</td>
</tr>
</tbody>
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## Summary of studies

### Depression as primary diagnosis

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<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Sample</th>
<th>Inclusion criteria</th>
<th>CAM Rx</th>
<th>Control Rx</th>
<th>Outcome measure(s)</th>
<th>Results</th>
<th>Methodology comments</th>
<th>Clinical comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heulluy 1985</td>
<td>RCT (non-blinded)</td>
<td>N= 60</td>
<td>‘Currently under consultation for depression, postmenopausal involution or thymo-effective dystonia’</td>
<td>Non – individualised L72 (constituents not specified) (twenty drops 4 times daily for 31 days) dose increased if required</td>
<td>Diazepam (dose and frequency unknown)</td>
<td>Ratio of pre and post scores for selected items on HAMD scale</td>
<td>L72 as effective as diazepam on all measures (thymo-effective, somatic and objective parameters)</td>
<td>Unknown method of randomisation, concealment of allocation, whether blinded (not attempted?), loss to follow-up/withdrawals, co-interventions, compliance</td>
<td>Intervention appropriate - Yes Control/placebo Appropriate - No/unclear Outcomes appropriate - No Diagnostic classification a problem</td>
</tr>
<tr>
<td>Katz et al (unpublished)</td>
<td>RCT pilot (triple arm parallel group) double-blind, double-dummy</td>
<td>N= 11</td>
<td>Major depressive episodes of moderate severity, duration 4+ wks, HAMD score 17+</td>
<td>Limited list of 30 remedies, trained homeopath using decision support software. Remedy unchanged, dilution and regime adjusted Duration: 12 weeks</td>
<td>Fluoxetine 20mg daily increased to 40mg after 4 wks if no improvement in HAMD score and no adverse effects</td>
<td>Primary: HAMD, CGI Secondary: SF12, QoL quest., WSDS, Pittsburgh Sleep Quality Index quest. Treatment credibility Side Effects checklist</td>
<td>Not reported due to low numbers</td>
<td>Planned methodology rigorous except for compliance (self-reported) and co-interventions (unknown). However recruitment was problematic (11 recruited) and loss to follow-up/withdrawals (6 completed)</td>
<td>Not sent for clinical commentary</td>
</tr>
</tbody>
</table>
### Homeopathy in depression table of studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Sample</th>
<th>Inclusion criteria</th>
<th>Homeopathy Rx</th>
<th>Control Rx</th>
<th>Outcome measure(s)</th>
<th>Results</th>
<th>Methodology comments</th>
<th>Clinical comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davidson et al 1997</td>
<td>UC study (best case series?)</td>
<td>N= 12 (3 with depression) US hospital or homeopathic hospital. Recruitment process unclear</td>
<td>Social phobia, panic disorder, residual attention-deficit hyperactivity disorder, major depression, chronic fatigue syndrome</td>
<td>Full psychiatric assessment and homeopathic interview then individualised prescribing</td>
<td>N/A</td>
<td>CGI plus self-rated SCL-90 in the hospital, BSPS in the medical practice. Measures taken at variable intervals</td>
<td>58% (7) recorded a 50% reduction on the CGI scale 50% (6) recorded a 50% reduction on the SCL-90 or BSPS scale Response in 2 out of 3 patients with major depression Negative outcomes: none reported</td>
<td>Not randomised, controlled or blinded. Compliance unknown Co-interventions – Drug and dose reported not frequency</td>
<td>Intervention appropriate Yes Control/placebo N/A Outcomes appropriate Yes Very relevant, excellent preliminary report</td>
</tr>
<tr>
<td>Clover et al 1995</td>
<td>UC study (consecutive case series)</td>
<td>N= 50 Referral to UK homeopathic hospital</td>
<td>Cancer-related symptoms (including mood disturbance)</td>
<td>Individualised homeopathy</td>
<td>None</td>
<td>HADS Rotterdam Symptom Checklist (RSCL) Initial, 2&lt;sup&gt;nd&lt;/sup&gt;, 3&lt;sup&gt;rd&lt;/sup&gt; and 4&lt;sup&gt;th&lt;/sup&gt; clinic attendances</td>
<td>Improvements on the psychological distress subscale of RSCL comparing initial scores with 3&lt;sup&gt;rd&lt;/sup&gt; and 4&lt;sup&gt;th&lt;/sup&gt; visits (p&lt;0.005 and &lt;0.02). Improvement in HADS Anxiety</td>
<td>Not randomised or blinded Loss to follow-up/withdrawals: 58% (29) reasons documented (15 died, 0 lost to follow-up) Co-interventions and other confounders: 29 (58%) prescribed SC</td>
<td>Intervention appropriate Yes Control/placebo N/A Outcomes appropriate Yes (for quality of life)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>N=</td>
<td>Referral</td>
<td>Duration</td>
<td>Outcome</td>
<td>Intervention</td>
<td>Control/placebo</td>
<td>Outcomes</td>
<td>Co-interventions and other confounders</td>
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<tr>
<td>Thompson and Reilly</td>
<td>UC study (consecutive case series)</td>
<td>100</td>
<td>Referral to UK homeopathic hospital cancer clinic</td>
<td>Sixty minute consultation and prescription of individualised remedy</td>
<td>Self-rating of symptoms on 11 point scale HADS EORTCQLQ-30</td>
<td>Initially 59 with anxiety, 37 with depression. For patients with at least 2 follow-ups mean anxiety scores improved by 1.6 (95%CI 0.4-2.9), mean depression scores improved by 1.4 (0.1-2.6)</td>
<td>Not randomised or blinded</td>
<td>Loss to follow-up/withdrawals: 44% 56 completed (26 died, 18 defaulted) Co-interventions and other confounders: unknown</td>
<td>Well-designed and pragmatic cohort study</td>
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<td></td>
<td></td>
<td>45</td>
<td>(26 from previous study) Outpatients at UK homeopathic hospital</td>
<td>60 minute consultation and Rx of individualised remedies (25 of variable potency, 30% as LM, for up to 3 symptoms). Pulsatilla,</td>
<td>Score of an effect on daily living of 3 symptoms (unvalidated) Scales were used at every consultation Symptom scores HADS</td>
<td>Significant improvement in all 3 main symptoms</td>
<td>Not randomised or blinded</td>
<td>Loss to follow-up/withdrawals: 11% 40 completed (1 died, 4 defaulted) Co-interventions and other confounders: conventional cancer treatment, (55% tamoxifen, 48%</td>
<td>Excellence case series/cohort study</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>N</td>
<td>Condition</td>
<td>Intervention</td>
<td>Control/placebo</td>
<td>Outcomes appropriate</td>
<td>Intervention appropriate</td>
<td>Quality</td>
<td></td>
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<tr>
<td>Zenner and Weisner 1999</td>
<td>UC study (prospective, multicentre outcome based)</td>
<td>269</td>
<td>Gynaecological disorders (including 102 with mood disorders)</td>
<td>Proprietary homeopathic remedy – Mulimen* given as drops (in 83% patients) or injection</td>
<td>N/A</td>
<td>Improvement in symptoms</td>
<td>Very good/good for between 75-80% cases for mood disorders (n=88)</td>
<td>Not randomised or controlled</td>
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<td>Patient and physician final evaluation on 5 point scale</td>
<td></td>
<td>Tolerance on 4 point scale</td>
<td>77% recorded good/very good improvement in symptoms</td>
<td>Loss to follow-up/withdrawals: results for 221/269 (82%) but response rate for questionnaire 28.5%</td>
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<td>Co-interventions and other confounders: 18% other medications, 2% other therapies</td>
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</tr>
</tbody>
</table>

* constituents: Ambra grisca 4X, Calcium carbonicum Hahnemannii 8X,, Cimicifuga racemosa 4X, Gelsemium sempervirens 4X, Hypericum perforatum 3X, Kalium carbonicum 4X, Sepia officinalis 8X, Urtica urens 3X, Vitex agnus-castus 3X

Abbreviations: RCT randomised controlled trial, CCT controlled clinical trial, UC uncontrolled, DARE Database of Reviews of Effects, H homeopathy, D diazepam, HAMD Hamilton Depression Scale, P placebo, F fluoxetine, CGI Clinical Global Impression, QoL quality of life, WSDS Work and Social Disability Scale, BSPS Brief Social Phobia Scale, SCL-90 outpatient psychiatric rating scale, HADS Hospital Anxiety and Depression Scale, RSCL Rotterdam Symptom Checklist, EORTCQLQ-30 European Organisation for Research and Treatment in Cancer – Quality of Life Questionnaire – Core 30,

Research on patient satisfaction and experience with the therapy
- No qualitative studies were located
- The following studies addressed patient satisfaction and/or used patient outcome measures
Homeopathy in depression table of studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thompson 2002</td>
<td>Questionnaire (as part of study above)</td>
<td>75% of patients regarded homeopathic treatment as having been helpful or very helpful for their symptoms</td>
</tr>
<tr>
<td>Thompson 2003</td>
<td>Questionnaire</td>
<td>90% of patients rated their satisfaction as 7 or above on a 10 point scale (0=completely dissatisfied; 10=completely satisfied). 67% of patients regarded the homeopathic approach as helpful, very helpful or extremely helpful for their symptoms. 21% valued talking about the problem above the remedy, 36% valued both equally, 43% valued the remedy above talking</td>
</tr>
</tbody>
</table>