

Scope of homoeopathy in the treatment of depression: A narrative synthesis

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Abstract

Background: Depression is a disorder of major public health importance, in terms of its prevalence and suffering, dysfunction, morbidity and economic burden. Depression is one of the most common conditions for which people seek homoeopathic treatment. **Objective:** This study is aimed to understand the scope of homoeopathy in depression based on the results of previous studies. **Methods:** A study was done to evince the scope of homoeopathic medicines in the treatment of depression. Searches were done in both general and specialised databases. The data were collected from peer-reviewed journals published between January 2001 and January 2021. Efforts were made to identify published articles on ‘depression and homoeopathy, homoeopathy for depression, depressive disorder and homoeopathy, dysthymia in homoeopathy’. **Results:** Twenty-one relevant studies were found and included in the review. These included systematic reviews, randomised control trials, observational studies, case series and case reports. Even though the studies considered in the review indicate the effectiveness of Homoeopathy, it is difficult to assess the overall effect of homoeopathy systematically, mostly because of compromised study designs. **Conclusion:** This review has helped in synthesising the existing literature on the scope of homoeopathy in the treatment of depression. However, in order to obtain more reliable results, better-designed researches, with long-term follow-ups may be planned.

Keywords: Depression, Depression rating scale, Homoeopathy, Mental Health, Narrative synthesis

INTRODUCTION

Depression (major depressive disorder [MDD] or clinical depression) is a common, but serious mood disorder.^[1] Mood and affect in depression are unreactive to circumstance, remaining low throughout the course of each day. In some people, mood varies diurnally, with gradual improvement throughout the day, only to return to a low mood on waking.^[2]

Research suggests that a mixture of genetic, biological, environmental and psychological factors play a role in depression.^[3] Depression can occur along with other serious diseases, such as diabetes, cancer, heart disease and Parkinson’s disease. Depression can make these conditions worse and vice versa. Sometimes, medications taken for these diseases may cause side effects that lead to depression symptoms.^[1]

According to the International Classification of Diseases (ICD)-10 classification of mental and behavioural disorders, depression includes depressive episodes (F32), recurrent depressive episodes (F33), persistent mood (affective) disorder (F34), other mood (affective) disorder (F38) and unspecified

mood disorder (F39).^[4] The diagnostic and statistical manual of mental disorders of the American Psychiatric Association, currently in its fifth edition, contains disruptive mood dysregulation disorder, MDD, persistent depressive disorder, premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder due to another medical condition and other specified depressive disorder.^[5]

A systematic analysis of the global burden of disease study from 2007 to 2017 estimated that depressive disorders along with low back pain and headache disorders are the three leading causes of years lived with disability (YLD). Between 1990 and 2007, the number of all-age YLDs attributable to depressive disorders increased by 33.4%.^[6]

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Received: 17 May 2021; **Accepted:** 06 December 2022

Access this article online

Quick Response Code:

Available in print
version only

Website:
www.ijrh.org

DOI:
10.53945/2320-7094.1070

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How to cite this article: Moorthi K, Radhika P, Chandran M, Muraleedharan KC. Scope of homoeopathy in the treatment of depression: A narrative synthesis. Indian J Res Homoeopathy 2022;16(4):269-281.

Due to their impact and widespread prevalence, depressive symptoms are a growing public health concern. Globally, more than 264 million people of all ages suffer from depression. When long-lasting and with moderate or severe intensity, depression may become a serious disorder. It can cause the affected person to suffer greatly and function poorly at work, at school and in the family. At its worst, depression can lead to suicide.^[6,7] Almost 1 million lives are lost yearly due to suicide, which amounts to 3000 suicide deaths every day.^[8]

Major depressive episode (MDE) includes depressive episodes that occur as part of a bipolar disorder, whereas MDD excludes bipolar depression. Because the vast majority of lifetime MDE is MDD, the difference between the two is not of great importance. However, bipolar depression is considerably more persistent than non-bipolar depression.^[9]

A meta-analysis of prospective cohort studies indicates that insomnia is significantly associated with an increased risk of depression.^[10] Research has also identified other risk factors for depression like cognitions and cognitive processes; stressors; certain sociodemographic factors, such as being female; parental depression and certain traits, behaviour patterns and dispositions.^[11]

Effective treatments are available both when depression occurs alone and when it co-occurs with general medical illnesses. Barriers to diagnosing and treating depression include stigma; patient somatisation and denial; physician knowledge and skill deficits; limited time; lack of availability of providers and treatments and restrictions on specialist, drug and psychotherapeutic care.^[12]

Dr Samuel Hahnemann (1796–1843), founder of Homoeopathy, was a pioneer in the diagnosis and classification of mental diseases. He advocated humane treatment for mental illness. He opposed the practice of chaining mental patients and granted respect to them which was revolutionary at its time.^[13] Homoeopathy states that the body and mind are integrated. According to the homoeopathic concept, physical disease can make changes in the mental/emotional state and vice versa. It attempts to go to the core of the disease in each individual patient. The ‘totality of symptoms’ in an individual patient comprises all changes observable on physical as well as mental/emotional sphere. A homoeopathic ‘similimum’ is the medicine that matches the totality of the patient’s physical and mental/emotional symptoms, irrespective of which came first.^[14]

Depression is one of the most common conditions for which people seek homoeopathic treatment.^[15] Various sorts of studies have evinced the scope of homoeopathy in mental diseases.^[16-19] We found that many studies showed efficacy in depression and the results are encouraging to collect cumulative evidence. This study is aimed to integrate the results of the previous studies, which have already assessed the efficacy of homoeopathy in depression, in a systematic way.

METHODS

Study design

The study was done based on critical assessment and evaluation of research articles, to provide an overview of the quality of the best available evidence of homoeopathic management of depression.

Search strategy and selection criteria

For the search and screening processes, we applied the PICO model, which considers four facets: Population, Intervention, Comparison and Outcomes.^[20] Search was done in both general and specialist databases such as psycINFO, Medline, PubMed, EMBASE, Cochrane library, CINHALL, Hom-inform, Complementary and Alternative Medicine and Wiley library. Literature searches were carried out by one researcher from 6 January 2021 to 10 January 2021, with an updated search from 13 January 2021 to 20 January 2021. Efforts were made to identify published articles on ‘depression in homoeopathy, homoeopathy for depression, MDD, MDE, depressive disorder and homoeopathy or dysthymia in homoeopathy’. There were 1236 hits which were then subject to various filtration criteria.

Inclusion criteria

Studies reporting the homoeopathic treatment of patients with depression or depressive disorder published in peer-reviewed journals between January 2001 and January 2021 were included, because of our interest in new literature. Adults of either sex with the primary diagnosis of depression or depressive disorder according to standard operationalised diagnostic criteria (Feighner criteria, research diagnostic criteria, diagnostic and statistical manual of mental disorders [DSM]-III, DSM-III-R, DSM-IV, DSM-5 and ICD-10) were included in the study. It included randomized controlled trials, cohort studies, prospective observational studies, case series, case reports, and also conference abstracts. Only the articles published in English were scrutinized. The studies which compared homoeopathic intervention with allopathic medicine, placebo or cognitive behavioural therapy were also included in this review. Homoeopathic interventions in all forms, such as individual and complex homoeopathic medicines, were included.

Exclusion criteria

Studies reporting depression with substance abuse, depression as a co-morbid disorder, and those having participants whose primary diagnosis was not depression or depressive disorder were excluded.

Outcome measures

Depression rating scales and standard measurements for sleep, satisfaction or quality of life were used wherever relevant. Beck inventory scale, Hamilton depression rating scale, Greene climacteric scale, Montgomery and Asberg depression rating scale, hospital anxiety and depression scale, Edinburgh postnatal depression scale, Columbia-Suicide Severity Rating Scale, Clinical Global Impression (CGI), Short-Form 12 (SF12), quality of life questionnaire and the Work and Social

Disability Scale (WSDS) and the Pittsburgh Sleep Quality Index questionnaire were used.

Data management

Both independent investigators reviewed full-text versions of the articles and articles were retained if they met the inclusion criteria. The agreement on inclusion and exclusion assignment was unanimous. Data collected using a tailored form was extracted from included studies. These comprised: authors; study design; intervention, original authors' conclusions about efficacy across study outcomes and adverse effects, if reported any. All data required to answer the study questions was available within the papers, so no contact with authors was necessary. The authors found that there was heterogeneity in the populations studied, the type of interventions offered, and the outcome measures reported. It was therefore methodologically inappropriate to combine most studies. Wherever applicable, the results of similar studies were pooled. The results were summarized in tables and text.

Quality assessment

Due to the heterogeneity of the type of studies, distinct assessment tools had to be used to assess the quality of the studies. Critical Appraisal Checklist developed by Critical Appraisal Skills Programme for systematic review, Newcastle–Ottawa Quality Assessment Scale for non-randomised studies, appraisal tool for cross-sectional studies (AXIS), Institute of Health Economics (IHE) Quality Appraisal Checklist for case series and Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Series are the tools used.^[21-25] After a thorough quality assessment, all quantitative data were generated and tabulated.

RESULTS

An adapted PRISMA flow diagram shows the process followed to select the studies used in this report [Figure 1].^[26] Nine databases and other sources identified 1236 titles. After the removal of duplicates, 386 titles were screened. Of these, 150 studies were deemed as potentially relevant and were reviewed

in detail. Finally, we excluded 129 irrelevant studies and 21 studies were included in the review.

Quality of included studies

It was intended that, based on the assessment criteria designated for each study in the respective tool, the studies were subdivided into three categories:

1. Mild: <50% of the quality criteria met.
2. Moderate: at least 50% of the quality criteria met.
3. High: more than 70% of the quality criteria met.

A summary of the included studies is reported below, and also in Table 1.

The systematic study on homoeopathy and depression by Pilkington *et al.* in 2005 stated that the effectiveness of homoeopathy in depression is limited due to a lack of high-quality clinical trials.^[27] Another systematic study by Viksveen *et al.* in 2018 assessed the efficacy, effectiveness and safety of homoeopathy in depression. Out of the 18 studies identified, limited evidence from two placebo-controlled double-blinded trials suggests that homoeopathic medicinal products might be comparable to antidepressants and superior to placebo in depression, and patients treated by homoeopaths report improvement in depression.^[28] Another semi-structured qualitative interview study was done by Viksveen *et al.* in 2017, within a randomised controlled trial to learn about depressed patients' experiences with the treatment provided by homoeopaths. Most of those interviewed were uncertain about how the treatment worked but described improvements in their mental and general state of health.^[29]

In a randomised controlled clinical trial, a 'cohort multiple randomised controlled trial' design was used to test the effectiveness of adjunct treatment by homoeopaths compared to usual care alone, over a period of 12 months in patients with self-reported depression. The primary outcome was measured through Patient Health Questionnaire (PHQ-9) tool and the authors conclude by stating that an offer of treatment provided

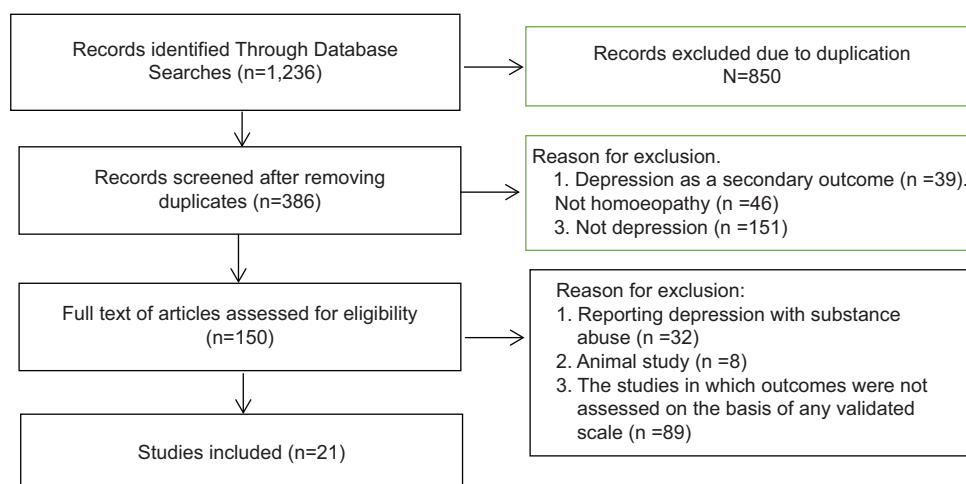


Figure 1: Flow chart depicting the study selection

Table 1: Summary of the included studies

S. No.	Article	Study design/sample size/instrument used	Quality	Strength	Limitation
1	Pilkington K, Kirkwood G, Rampes H, Fisher P, Richardson J. Homoeopathy for depression: A systematic review of the research evidence. <i>Homoeopathy</i> . 2005 Jul; 94 (3):153-63. doi: 10.1016/j.homp. 2005.04.003. PMID: 16060201	CASP-systematic study review	High	The review addressed a clearly focused issue. The review included the right type of papers. The quality of the studies was assessed properly	The results were not combined, because of the heterogeneity of the studies
2	Viksveen P, Fibert P, Relton C. Homoeopathy in the treatment of depression: A systematic review. <i>European journal of integrative medicine</i> . 2018;22:22-36.	CASP-systematic study review	Moderate	The review addressed a clearly focused issue. The right type of papers was selected. The results of the review are explicitly stated and it can be applied to the local population. The risk of bias was assessed according to the Cochrane Collaboration's guidelines, focusing on the main outcome measure for each trial. The potential risk between study – publication bias was also considered. The review used a novel approach to the assimilation of evidence by considering three different types of evidence: Those assessing the efficacy of homoeopathic medicines; those assessing the effectiveness of treatment by homoeopaths and those describing the outcomes of patients treated by homoeopaths.	Quality assessments not done. aggregated results can be presented in limited extent due to the heterogeneity of studies
3	Adler UC, Paiva NM, Cesar AT, Adler MS, Molina A, Padula AE, Calil HM. Homoeopathic individualised Q-potencies versus fluoxetine for moderate to severe depression: Double-blind, randomised non-inferiority trial. <i>Evid Based Complement Alternat Med</i> . 2011;2011:520182. doi: 10.1093/ecam/nep114.	CASP-randomised trial. Sample size 91. The study was a prospective, randomised, double-blind, double-dummy trial, with fluoxetine as the active control	High	It was a non-inferiority trial. It was double-blinded, double-dummy and placebo-controlled trial. Results state that homoeopathy is non-inferior to fluoxetine. All patients underwent the same medical and homoeopathic assessment. Both groups (homoeopathy $n = 48$, fluoxetine $n = 43$) improved over time ($P < 0.001$) on the Montgomery and Åsberg Depression Rating Scale (MADRS), with no significant between-group differences at 4 weeks (95% CI-6.95, 0.86, $P=0.65$) and 8 weeks (95% CI-6.05, 0.77, $P=0.97$). The pre-fixed margin of non-inferiority was (Δ) 1.45, which was 1/3–1/2 of the advantage of fluoxetine over placebo, and the minimum considered clinical relevance. The sample size was sufficient to establish the non-inferiority of homoeopathy compared to fluoxetine.	Only percentages (and not numbers) were provided for secondary outcomes. The trial had high risk of bias due to high attrition rates (40% in both trial arms) and acceptable model validity.
4	Viksveen P, Relton C, Nicholl J. Depressed patients treated by homoeopaths: A randomised controlled trial using the 'cohort multiple randomised controlled trial' (cmRCT) design. <i>Trials</i> . 2017;18 (1):299.	CASP-randomised trial. The sample size of 485 patients. Cohort multiple randomised controlled trial (cmRCT) design	Mild	The trial addressed a clearly focused issue. All the patients were randomised into groups. The use of the cmRCT design provides the additional benefit of testing the acceptability of the intervention. Questionnaires were, however, completed by patients at home, thereby avoiding any undue research influence on patients	Less number of participants was in the adjuvant group than the control group. Another limitation of this trial was a lower 6-month and 12-month questionnaire response rate in patients who were randomly selected to be offered the intervention, but who did not take up the offer.

(Contd...)

Table 1: (Continued)

S. No.	Article	Study design/sample size/instrument used	Quality	Strength	Limitation
					Another limitation was the lack of blinding. Potential non-acceptance of an offer of treatment is a specific feature of the cmRCT design that warrants particular attention when interpreting trial results. The confidence interval precludes any firm conclusions from being drawn.
5.	Văcăraș V, Vithoulkas G, Buzoianu AD, Mărginean I, Major Z, Văcăraș V, <i>et al.</i> Homoeopathic treatment for postpartum depression: A case report. <i>Journal of evidence-based complementary and alternative medicine.</i> 2017 Jul; 22 (3):381-4.	JBI-case report	Moderate	The dramatic improvement in the patient's condition with the use of homoeopathic medication was corroborated by all parameters evaluated by the 3 scales routinely used both in this department and in this case. The patient had improvement in functional level too	The patient's demographic characteristics are not clearly described. The patient's history is not clearly described nor presented as a timeline. The current clinical condition of the patient on presentation is clearly described. The assessment methods and the results are not clearly described. The interventions are clearly described. The post-intervention clinical condition is not clear. Adverse events are not mentioned
6.	Moorthi SK. Homoeopathic treatment for Severe Depression with Psychotic features. <i>International Journal of Homoeopathic Sciences.</i> 2020;4 (1):82-86.	JBI-case report	Moderate	The history of the patient is well depicted. The current clinical condition of the patient on presentation is clearly described. The assessment methods, results and interventions are clearly described in tables. Improvements were measured with scales. Patients had improved in their functional level too	The patient's demographic characteristics are not clearly described. Adverse events are not mentioned
7.	Bagherian M, Mojembari AK, Hakami M. The effects of homeopathic medicines on reducing the symptoms of anxiety and depression: Randomized, double blind and placebo controlled. <i>J Homeopath Ayurv Med</i> 2014;3:167-1206.	CASP-randomised trial. Sample size-30. Randomised, double-blind and placebo-controlled trial	Mild	A true representative sample is used. Non-exposed cohorts are drawn from different sources. Ascertainment of exposure is from a secure record. Demonstrated that the outcome of interest was not present at the start of the study. The outcome was assessed by Hospital Anxiety and Depression Scale, HAD. Follow-up was long enough	No selection criteria applied prior to the invitation to join this cohort study. Participation rate was very low. There was potential selection bias
8.	Adler UC, Krüger S, Teut M, <i>et al.</i> Homoeopathy for depression: A randomised, partially double-blind, placebo-controlled, four-armed study (DEP-HOM). <i>PLoS One.</i> 2013;8 (9):e74537. Published 2013 Sep 23. doi: 10.1371/journal.pone. 0074537.	CASP-randomised trial. Sample size-44. A randomised, partially double-blind, placebo-controlled, four-armed study	High	The trial addresses a clearly focused issue. Patients were properly randomised to provide treatment. All the patients who entered the trial were not accounted for at its conclusion. The results can be applied to the local population. All clinically important outcomes were considered	It was a partially double-blind study. The groups were not similar at the start of the trial. Aside from the experimental intervention, the groups were not treated equally. Only an exploratory analysis was done
9.	Macías-Cortés Edel C, Llanes-González L, Aguilar-Faisal L, Asbun-Bojalil J. Individualised homoeopathic treatment and fluoxetine for	CASP-randomised trial. Sample size-133.	Mild	Diagnosed with major depression according to DSM-IV. Moderate-to-severe depression was measured according with 17-item HRSD. Beck Depression Inventory and Greene Climacteric Scales were	This article has been retracted. Retraction in: <i>PLoS One.</i> 2020 April 23; 15 (4): e0232415.

(Contd...)

Table 1: (Continued)

S. No.	Article	Study design/sample size/instrument used	Quality	Strength	Limitation
	moderate to severe depression in peri- and postmenopausal women (HOMDEP-MENOP study): A randomised, double-dummy, double-blind, placebo-controlled trial (retracted in: PLoS One. 2020 Apr 23;15 (4):e0232415). PLoS One. 2015;10 (3):e0118440. Published 2015 Mar 13. doi: 10.1371/journal.pone.0118440	A randomised, double-dummy, double-blind, placebo-controlled trial		used. A randomised, double-dummy, double-blind, placebo-controlled trial	The individualised homoeopathic treatment and the decision-making framework for treatment adjustments were not reported in sufficient detail. The study design did not include sufficient controls
10.	Katz T, Fisher P, Katz A, Davidson J, Feder G. The feasibility of a randomised, placebo-controlled clinical trial of homoeopathic treatment of depression in general practice. <i>Homoeopathy</i> . 2005;94 (3):145-52.	CASP-randomised trial. Sample size-23. Randomised, double-dummy, double-blind parallel group clinical trial. Setting:	Mild	The study addressed a clearly focused research question. The assignment of participants to interventions was randomised. All participants who entered the study were not accounted for at its conclusion	Methodology was well planned and rigorous. However, cointerventions are unknown. However, recruitment was scarce and loss to follow-up/withdrawals were more
11.	Oberai P, Balachandran I, Janardhanan Nair KR, Sharma A, Singh VP, Singh V, Nayak C. Homoeopathic management in depressive episodes: A prospective, unicentric, non-comparative, open-label observational study. <i>Indian J Res Homoeopathy</i> 2013;7:116-25.	Observational studies, based on the Newcastle–Ottawa scale Sample size-83. A prospective, unicentric, non-comparative, open-label observational study	Moderate	The intensity of depression was measured using validated scales such as Hamilton Depression Rating Scale (HDRS) and Beck Depression Inventory (BDI). Other assessment measures were the Clinical Global Impression (CGI-1) scale. A validated measure of illness severity and Clinical Global Improvement (CGI-2) owing to treatment. The data relating to these questionnaires were collected at baseline and at monthly intervals for 12 months by the investigators and consultant psychiatrist. The ITT principle was applied for conducting the analysis	Confounding factors are not explained or not accounted in the design and/or analysis. Follow-up of this study was short.
12.	Novak MR. Integrative sulphiride with a homoeopathic therapy for treating depressive syndrome – An observational study. <i>Psychiatria Danubina</i> , 2011;23 (2):200-201.	Observational studies, based on the Newcastle–Ottawa scale. Sample size-82. An observational study.	Mild	Improvements were assessed with HDRS scale.	No information regarding the effectiveness of specific homoeopathic remedies and potencies. The duration of the study was too short. A detail of participants was not explicitly mentioned. Not provided the details of adverse effects. The details of the study design were not provided
13.	del Carmen Macías-Cortés Macías-Cortés E, Llanes-González González L, Aguilar-Faisal L, Asbun-Bojalil J. Response to individualised homoeopathic treatment for depression in climacteric women with a history of domestic violence, marital dissatisfaction or sexual abuse: Results from the HOMDEP-MENOP study. <i>Homoeopathy</i> . 2018 Aug; 107 (03):202-8.	CASP-randomised trial. Sample size-133. A randomised, placebo-controlled, double-blind, double-dummy, three-arm trial follow-up study	High	The severity of symptoms was determined with two well-known standardised scales used. Risk factor for depression was assessed	The mental health examination and any standardised tool did not specifically used for evaluating DV, SA or MD. First, sample size was calculated for the primary analysis, aiming to detect an effect size

(Contd...)

Table 1: (Continued)

S. No.	Article	Study design/sample size/instrument used	Quality	Strength	Limitation
14.	Grimaldi-Bensouda L, Abenham L, Massol J, Guillemot D, Avouac B, Duru G, et al. Homoeopathic medical practice for anxiety and depression in primary care: the EPI3 cohort study. BMC Complement Altern Med. 2016;16:125. doi: 10.1186/s12906-016-1104-2. PMID: 27145957; PMCID: PMC4855343.	Newcastle–Ottawa Quality Assessment Scale. Sample size-1562. Cohort study.	Moderate	Variety of information collected at baseline, covering sociodemographic and clinical characteristics. No instructions were given to participating physicians or patients to prevent interference. Three groups were free to prescribe conventional and/or homoeopathic drugs. Hospital Anxiety and Depression Scale (HADS) questionnaire had used.	Diagnoses of disease symptoms were based on own clinical judgement, of general practitioners with no attempt at standardisation or external validation or participation rate
15.	Mahwish N, Mehmood A, Nauman AT. A study on the curative action of <i>Arsenicum album</i> in major depression. European Journal of Integrative Medicine. 2010;4 (2):226-7.	JBICross-sectional studies. It is a cross-sectional qualitative and quantitative research work. Sample size-200 patients.	Low	The approach of a single remedy	Particular medicine and particular potency were used for all the participants without any clear evidence. Assessment of symptom reductions was not mentioned
16.	Grimaldi-Bensouda L, Engel P, Massol J, Guillemot D, Avouac B, Duru G, et al. who seek primary care for sleep, anxiety and depressive disorders from physicians prescribing homoeopathic and other complementary medicine? Results from the EPI3 population survey. BMJ open. 2012;2:e001498.(6).	Observational studies, based on the Newcastle–Ottawa scale observational study. Sample size-1572.	High	High representativeness of the patients. Quality assessment is done.	The design does not allow for addressing the directionality of the associations described between patients' characteristics and their physician's choice of medical practice. The participants recruited in primary care might have excluded people with severe psychiatric disorders. This potential bias was likely to underestimate the prevalence of psychotropic drug use
17.	Mathie RT, Robinson TW. Outcomes from homoeopathic prescribing in medical practice: A prospective, research-targeted, pilot study. Homoeopathy. 2006;95 (4):199-205.	A prospective, research-targeted, pilot study	-	Sample size-88. Method of spreadsheet done properly. Patient-assessed outcome by 7-point Likert scale	The most common difficulty was in cases where a patient presented with two discrete medical conditions that were treated separately with two different homoeopathic medicines. The study duration was brief. The rating scale for depression was not used
18.	Itamura R. Homoeopathy for thirteen chronic depression patients. Integr Med Res 2015;4:25-6.	IHE quality Appraisal Checklist for case series. Thirteen patients were treated.	Mild	Follow-up was long enough	Assessment is not mentioned. Characteristics of the patients are not mentioned. Recruitment details are not mentioned.
19.	Adler UC, Paiva NM, CeasarCesar AD, Adler MS, Molina A, Calil HM. Homoeopathic treatment of depression: Series of case report. Archives of Clinical Psychiatry (São Paulo). 2008;35 (2):74-8.	IHE Quality Appraisal Checklist for case series. Fifteen patients were treated. MADR scale was used	Mild	Validated scale was used	The study was not done prospectively. Statistical tests were not used. Follow-ups were not long enough

by homoeopaths for patients with self-reported depression was associated with a small treatment effect over a time period of 6–12 months, whereas a moderate effect was found in patients

who received treatment. However, wide confidence intervals preclude any firm conclusions from being drawn. Fourteen adverse effects were also noticed.^[29]

Another trial conducted by Adler *et al.* in 2011 aimed to investigate the non-inferiority and tolerability of individualised homeopathic medicines (Quinquagintamillesimal [Q-potencies]) in acute depression, using fluoxetine as an active control. This study indicated the non-inferiority of individualised homeopathic Q-potencies as compared to fluoxetine in the acute treatment of outpatients with moderate-to-severe depression.^[30]

Further, among the five placebo-controlled randomized trials identified for this review is a feasibility trial that was conducted by T Katz *et al.* to assess the feasibility of a general practice-based clinical trial comparing the effectiveness of individualised homeopathic treatment versus fluoxetine (Prozac) versus placebo in the treatment of MDEs of moderate severity. It displayed that a trial of this design in general practice is not feasible because of recruitment difficulties, many of them linked to patient preference.^[31]

A randomised, partially double-blind, placebo-controlled, four-armed study, by Adler *et al.*, was terminated because of recruitment problems.^[32] A randomised, double-blind and placebo-controlled was done by Bagherian *et al.*; findings exhibit that homeopathic therapy can be used as an effective method to treat depression disorders.^[33] A randomised, double-dummy, double-blind, placebo-controlled trial, which was conducted by Macías-Cortés *et al.* to assess the efficacy and safety of individualised homeopathic treatment versus placebo and fluoxetine versus placebo in peri- and postmenopausal women with moderate-to-severe depression shown that the homeopathic group was more effective than placebo.^[34] In 2018, a randomised, placebo-controlled, double-blind, double-dummy, three-arm trial on HOMDEP-MENOP study was conducted by Macías-Cortés who had shown a statistically significant association with response to depression treatment.^[35]

Seven observational studies identified were highly heterogeneous and could be presented in an aggregated form only to a limited extent. The objectives and outcomes used were combined and standard reporting guidelines for observational studies were followed by only a few of these. Both classical homeopathy and adjuvant treatment with the standard treatment showed clinical improvement, as well as on the standard scales Hamilton Depression Rating Scale (HDRS), Beck Depression Inventory (BDI) and Clinical Global Impression.^[18,36-41]

RT Mathie *et al.* conducted a pilot data collection study, in which 14 homeopathic physicians collected clinical and outcomes data over a 6-month period in their practice setting. A total of 1783 individual patient conditions were treated overall. The outcome from two or more homeopathic appointments per patient condition was obtained in 961 cases (75.9% positive, 4.6% negative, 14.7% no change; 4.8% outcome not recorded). Strongly positive outcomes were achieved most notably in anxiety, and depression.^[42]

A semi-structured qualitative interview study was done within a randomized controlled trial to learn about depressed patients' experiences with the treatment provided by homeopaths. Patients were interviewed to recall from their experiences with the intervention and to compare their experiences with antidepressants and other depression interventions. This qualitative study provided the first understanding of depressed patients' experiences with the treatment provided by homeopaths as an adjunct to usual care. Their experiences with the consultation were described through themes such as caring support and trust, and shared several similarities with "talking therapy" interventions. The results of this research may be of relevance to patients and providers considering homeopathic treatment for depressed patients.^[43]

The case series by R. Itamura stated that 13 patients had a significant process of cure from chronic depression through homeopathy for 2 years. All patients were diagnosed as having MDDs with the DSM-IV and treated already several antidepressants. Cases were considered recovered when antidepressants had been stopped for 6 months and 3 months had passed since the stopping of homeopathic medicines.^[44]

Another one by Adler *et al.* in 2008, with the objective to report preliminary results of homeopathic treatment of depression in Jundiaí's public health system, Sao Paulo. The medical records of patients who received individualised homeopathy treatment for depression in between March and December 2006 were reviewed. The outcome and symptoms severities were measured with Montgomery and Åsberg Depression Scale (MADRS). Fifteen patients were treated and response (more than 50% decrease of MADRS scores) was observed in 14 patients (93%), after an average of 7 weeks of treatment; one patient had clinical worsening and the remaining patients' results were significant.^[45]

A case report of postpartum psychosis showed significant improvement. The Edinburgh postnatal depression scale, positive and negative syndrome scale and global assessment of functionality scale were used to measure clinical outcomes in symptom severity and treatment efficacy in subjects with psychoses.^[46] Another case presented with severe depression with psychosis symptoms. Hamilton Depression Rating Scale and Brief Psychiatric Rating Scale were used to measure the clinical outcome and symptom severity. The patient had significant improvement in social life and functioning with standalone homeopathic treatment. Even the acute exacerbation was also managed with individualised homeopathic medicine during the depressive episode.^[47]

DISCUSSION

This review provides a comprehensive overview of the evidence of Homeopathy in treatment of Depression. All attempts were made to recover both published peer-reviewed studies and reports available online. The authors assure that the entire relevant literature available in English language, within the specified time, was identified for the

review, though it is expected that some studies might have got missed inadvertently. Also, the extent of missing data from unpublished studies is not known. Although the review found substantial clinical trial literature, the presence of basic methodological weaknesses and of comorbidities in the recruited participants led to the exclusion of many studies. The results for non-English studies were not considered, which might have led to selection bias. The studies published in non-peer-reviewed journals were also excluded. Such studies provide only relatively weak evidence of effectiveness. Hence, only the studies fulfilling the inclusion criteria were assessed. It is also pertinent to mention that three RCTs included in this study were also a part of the two systematic reviews included for the present synthesis.^[27,28,30-32]

Based on the assessment criteria, the studies were subdivided into mild, moderate and high categories. It may be noted that this quality assessment was specific to each paper regardless of the paper type. Hence, one may observe that an RCT has scored a mild or moderate grade, while a case report has scored a high grade. Quality assessment of three studies could not be done due to their heterogeneity.

The trials selected for the synthesis were entirely heterogeneous, as reported earlier, in terms of the type of homoeopathy used, outcome measures, types of depression, methodological qualities, risk of bias and quality of individualisation. There were trials assessing the efficacy of homoeopathic medicines; those assessing the effectiveness of treatment by homoeopaths and those describing the outcomes of patients treated by homoeopaths.

The outcome measures were used to measure the reliability of responses and assist in objective assessment, diagnosis and monitoring of the patient outcome. These scales can easily be incorporated into clinical practice, which would help in following the progression of symptoms and the effectiveness of treatment.

Individualised homoeopathy was used in 13 studies, and single medicine *Arsenicum album* in 1 study, and complex homoeopathic remedies in another study. Even though three different prescribing strategies were used in the included studies i, positive results were obtained from all three. It is difficult to construct an analysis from the same. The uncontrolled studies were of poor quality, most of them not mentioning the methods, assessment tools, type of intervention and severity of depression of the population under study.

The RCTs, even though with differing risks of bias and model validity, provide evidence that homoeopathy has a positive role in the treatment of homoeopathy.

However, overall, the review shows that there is a paucity of high quality literature on Homoeopathy in depression. Most of the studies fall under the moderate and mild qualities of evidence. The most common reasons for the studies categorized as mild were inadequate sample size, short duration, poor description of the methods used, deviation from standard

criteria for grouping the samples, unequal ratio of sample size, and inadequate details of the questionnaires and scales used. Some studies have not used standardised and valid scales. Some studies had used substandard methods of treatment^[36] while the results of some of the studies appeared hard to accept.^[39] The standard guidelines may improve the content of the research, improve the utility of the research report and reduce the bias. From the limitations mentioned, researchers can avoid potential mistakes. The understanding of the scope, limitations and prognosis of individualised as well as add-on homoeopathic treatment in depressive disorder, can influence the treatment of homoeopathic practitioners.

Depression, being a common and recurrent disorder, needs long-term follow-ups. None of the studies had a long-term assessment, reasonable enough to state that homoeopathy has a curative and preventive effect on depression. The diagnostic criteria were only clearly mentioned in eight studies (either ICD or DSM).

Only two randomised active control trials and five placebo-controlled trials made it to the final inclusion. The authors found that most of them were not following the Consolidated Standards of Reporting Trials (CONSORT).^[48] Only two out of the seven studies had a sample size above 100.^[34,35] Less number of participants was one of the main drawbacks that could be identified. One study, however, which was terminated due to poor recruitment had a robust research design.^[32] Six out of seven RCTs had proper blinding strategies. Randomisation was done adequately in six studies. Allocation concealment was mentioned properly in two studies. Among all RCTs, the maximum duration of the study was 9 months, which was seen in two studies.

Implications for clinical practice

Even though the individualised homoeopathic approach often yields good clinical results, it has not yet been able to render positive outcomes in the scientific literature because of a myriad of methodological weaknesses. Thus, the evidence underpinning the usefulness of homoeopathy in depression remains unconvincing, even though these studies, when considered separately, seem to make a reliable statement. Two following studies not considered in this review have similar outcomes. An observational survey conducted in France between 2007 and 2008, on the patients with depressive disorders has shown a positive effect of homoeopathy in its effectiveness and lower psychotropic drug use.^[40]

Statistical analysis of 156 cases of depression treated with classical homoeopathy selected from Vithoulkas Compass online homoeopathic software and women reported a better response to homoeopathy.^[37]

Implications for future research

As narrated above, the currently available literature in homoeopathy has a lucid theoretical framework that could be used as the foundation for experimental studies to examine their effect. Most of the studies have very poor adherence to

reporting guidelines. It is recommended that authors, reviewers and editors comply with available reporting guidelines suitable for homeopathic trials (HOM CASE, etc.). Furthermore, the standard guidelines and tools, as applicable, should be utilised during protocol development.

Collaborative multicentric trials to evaluate the safety, feasibility and efficacy of the homeopathic intervention in treating various stages and severity of depression is the need of the hour. Experimental studies, with robust methodologies and validated intervention protocols, are lacking and are warranted in future. High-quality, non-inferiority or equivalence efficacy and safety trials evaluating Homeopathy as a treatment option as a standalone or adjuvant, may be designed for drawing conclusions.

CONCLUSION

This review is an attempt in synthesising the existing literature on the effectiveness of homeopathy in the treatment of depression. However, to obtain more reliable results, further research may be better designed, with long-term follow-ups. It is also suggested that future efforts also emphasise the adverse effects, as much as they emphasise the efficacy of homeopathic treatment.

Financial support and sponsorship

Nil.

Conflicts of interest

None declared.

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Portée de l'homéopathie dans le traitement de la dépression: Une synthèse narrative

Contexte: La dépression est un trouble d'une importance majeure pour la santé publique, en termes de prévalence et de souffrance, de dysfonctionnement, de morbidité et de charge économique. La dépression est l'une des affections les plus courantes pour lesquelles les gens recherchent un traitement homéopathique. **Objectif:** Cette étude vise à comprendre la portée de l'homéopathie dans la dépression en se basant sur les résultats des études précédentes. **Méthodes:** Une étude a été réalisée afin d'évoquer la portée des médicaments homéopathiques dans le traitement de la dépression. Des recherches ont été effectuées dans des bases de données générales et spécialisées. Les données ont été collectées dans des journaux évalués par des pairs et publiés entre janvier 2001 et janvier 2021. Des efforts ont été faits pour identifier les articles publiés sur "la dépression et l'homéopathie", "l'homéopathie pour la dépression", "le trouble dépressif et l'homéopathie", et "la dysthymie en homéopathie". **Résultat:** Vingt et une études pertinentes ont été trouvées et incluses dans l'examen. Il s'agissait de revues systématiques, d'essais contrôlés randomisés, d'études d'observation, de séries de cas et de rapports de cas. Même si les études prises en compte dans l'examen indiquent l'efficacité de l'homéopathie, il est difficile d'évaluer l'effet global de l'homéopathie de manière systématique, principalement en raison des conceptions d'étude compromises. **Conclusion:** Cette revue a permis de synthétiser la littérature existante sur la portée de l'homéopathie dans le traitement de la dépression. Cependant, afin d'obtenir des résultats plus fiables, des recherches mieux conçues, avec des suivis à long terme, peuvent être planifiées.

Der Anwendungsbereich der Homöopathie bei der Behandlung von Depressionen: Eine erzählerische Synthese

Hintergrund: Depressionen sind eine Erkrankung, die aufgrund ihrer Prävalenz, ihres Leidens, ihrer Dysfunktion, ihrer Morbidität und ihrer wirtschaftlichen Belastung von großer Bedeutung für die öffentliche Gesundheit ist. Depressionen sind eine der häufigsten Erkrankungen, bei denen Menschen eine homöopathische Behandlung suchen. **Zielsetzung:** Ziel dieser Studie ist es, den Anwendungsbereich der Homöopathie bei Depressionen auf der Grundlage der Ergebnisse früherer Studien zu verstehen. **Methoden:** Es wurde eine Studie durchgeführt, um den Anwendungsbereich homöopathischer Arzneimittel bei der Behandlung von Depressionen aufzuzeigen. Es wurde sowohl in allgemeinen als auch in spezialisierten Datenbanken recherchiert. Die Daten wurden in begutachteten Fachzeitschriften gesammelt, die zwischen Januar 2001 und Januar 2021 veröffentlicht wurden. Es wurde versucht, veröffentlichte Artikel zu den Themen "Depression und Homöopathie", "Homöopathie bei Depressionen", "Depressive Störungen und Homöopathie" und "Dysthymie in der Homöopathie" zu finden. **Ergebnis:** Es wurden einundzwanzig relevante Studien gefunden und in die Überprüfung einbezogen. Dazu gehörten systematische Übersichten, randomisierte Kontrollstudien, Beobachtungsstudien, Fallserien und Fallberichte. Auch wenn die in der Übersichtsarbeit berücksichtigten Studien auf die Wirksamkeit der Homöopathie hinweisen, ist es schwierig, die Gesamtwirkung der Homöopathie systematisch zu bewerten, vor allem wegen der unzureichenden Studiendesigns. **Schlussfolgerung:** Diese Übersichtsarbeit hat dazu beigetragen, die vorhandene Literatur über den Anwendungsbereich der Homöopathie bei der Behandlung von Depressionen zusammenzufassen. Um jedoch verlässlichere Ergebnisse zu erhalten, sollten besser konzipierte Studien mit langfristiger Nachbeobachtung geplant werden.

अवसाद की चिकित्सा में होम्योपैथी का दायरा: एक वृत्तांत संकलन

पृष्ठभूमि: अवसाद व्यापकता एवं पीड़ा, शिथिलता, रुग्णता और आर्थिक बोझ के संदर्भ में प्रमुख सार्वजनिक स्वास्थ्य महत्व का विकार है। अवसाद सबसे आम स्थितियों में से एक है जिसके लिए लोग होम्योपैथिक उपचार चाहते हैं। **उद्देश्य:** इस अध्ययन का उद्देश्य पिछले अध्ययनों के परिणामों के आधार पर अवसाद में होम्योपैथी के दायरे को समझना है। **विधि:** अवसाद के उपचार में होम्योपैथिक दवाओं के दायरे को स्पष्ट करने के लिए एक अध्ययन किया गया था। खोज सामान्य और विशेष दोनों डेटाबेस में की गई। जनवरी 2001 से जनवरी 2021 के बीच प्रकाशित शिष्ट समीक्षा पत्रिकाओं से जानकारी एकत्र की गयी। "अवसाद और होम्योपैथी", "अवसाद के लिए होम्योपैथी", "अवसादग्रस्तता विकार और होम्योपैथी" और "मानसिक कष्ट में होम्योपैथी" पर प्रकाशित लेखों की पहचान करने का प्रयास किया गया। **परिणाम:** इक्कीस प्रासंगिक अध्ययन पाए गए और समीक्षा में शामिल किए गए। इनमें व्यवस्थित समीक्षा, यादृच्छिक नियंत्रण परीक्षण, अवलोकन संबंधी अध्ययन, विषय श्रृंखला और विषय व्याख्या शामिल हैं। भले ही समीक्षा में किए गए अध्ययनों से होम्योपैथी की प्रभावशीलता का संकेत मिलता है, परंतु अधिकांशतः दोषयुक्त अध्ययन संरचना के कारण होम्योपैथी के समग्र प्रभाव का व्यवस्थित रूप से मूल्यांकन करना मुश्किल है। **निष्कर्ष:** इस समीक्षा ने अवसाद के उपचार में होम्योपैथी के दायरे पर मौजूदा साहित्य को संश्लेषित करने में मदद की है। परंतु, अधिक विश्वसनीय परिणाम प्राप्त करने के लिए, लंबी अवधि के परामर्श के साथ-साथ बेहतर अध्ययन संरचना किए गए अनुसंधानों की योजना बनाई जा सकती है।

Alcance de la Homeopatía en el Tratamiento de la Depresión: Una Síntesis Narrativa

Fundamento: La depresión es un trastorno de gran importancia para la salud pública, en términos de prevalencia y sufrimiento, disfunción, morbilidad y carga económica. La depresión es una de las condiciones más comunes para las cuales las personas buscan tratamiento homeopático. **Objetivo:** El objetivo de este estudio es comprender el alcance de la homeopatía en la depresión a partir de los resultados de estudios previos. **Métodos:** Se realizó un estudio para descubrir el alcance de los medicamentos homeopáticos en el tratamiento de la depresión. Las búsquedas se realizaron tanto en bases de datos generales como especializadas.

Los datos se recopilaban de revistas revisadas por expertos publicadas entre enero de 2001 y enero de 2021. Se procuró identificar artículos publicados sobre “depresión y homeopatía”, “homeopatía para la depresión”, “trastorno depresivo y homeopatía” y “distimia en la homeopatía”. Resultado: Se encontraron 21 estudios relevantes que se incluyeron en la revisión. Estas incluyeron revisiones sistemáticas, ensayos de control aleatorios, estudios observacionales, series de casos e informes de casos. Aunque los estudios considerados en la revisión indican la eficacia de la homeopatía, es difícil evaluar sistemáticamente el efecto general de la homeopatía, sobre todo debido a diseños de estudio comprometidos. **Conclusión:** Esta revisión ha ayudado a sintetizar la literatura existente sobre el alcance de la homeopatía en el tratamiento de la depresión. Sin embargo, para obtener resultados más confiables, se pueden planificar investigaciones mejor diseñadas, con seguimiento a largo plazo.

顺势疗法治疗抑郁症的范围。叙述性综述

背景介绍: 抑郁症是一种具有重大公共卫生意义的疾病, 就其发病率和痛苦、功能障碍、发病率和经济负担而言。抑郁症是人们寻求顺势治疗的最常见情况之一。目标: 本研究旨在根据以往的研究结果, 了解顺势疗法在抑郁症中的应用范围。方法: 进行了一项研究, 以显示同种疗法药物在治疗抑郁症方面的作用。在一般和专门的数据库中都进行了搜索。数据收集自2001年1月至2021年1月期间出版的同行评议的期刊。我们努力寻找已发表的关于“抑郁症和顺势疗法”、“顺势疗法治疗抑郁症”、“抑郁症和顺势疗法”以及“顺势疗法中的抑郁症”的文章。结果: 发现了21项相关研究, 并将其纳入综述。这些研究包括系统回顾、随机对照试验、观察性研究、系列病例和个案报告。即使审查中所考虑的研究表明了顺势疗法的有效性, 但很难系统地评估顺势疗法的整体效果, 主要是因为研究设计受到了影响。总结: 本综述有助于综合现有文献, 了解顺势疗法在治疗抑郁症方面的范围。然而, 为了获得更可靠的结果, 可以计划进行设计更好的研究, 并进行长期的跟踪调查。