Characteristics of included studies	Allergy		
Study ID	**Aabel 2000a**		
Study reference	Aabel S, Laerum E, Dolvik S, Djupesland P. Is homeopathic 'immunotherapy' effective? A double-blind, placebo-controlled trial with the isopathic remedy Betula 30c for patients with birch pollen allergy. British Homeopathic Journal. 2000;89(4):161-8.		
Study design	RCT	Each centre received tablet vials randomly coded with a number. Vials were sent to a statistician for random coding.	
Author affiliation	Institute of General Practice and Community Medicine, Department of General Practice,Oslo, Norway; and Department of Otorhinolaryngology, Ullevaal University Hospital, Oslo, Norway		
Source of funds	Financed by the Research Council of Norway,The homeopathic remedy and placebo tablets were a gift from DCG, Gothenburg, Sweden		
Declared interests of study authors	Not reported		
Setting / provider	Community setting		
Country(s) / region	Oslow, Norway		
Enrolment period	27 April to 28 May 1995 (Birch pollen season) Oslo		
Length of intervention + follow up	4 wks, no follow up reported		
Description of population	*N=*	*Description*	
participants	70	Birch pollen allergy	

Characteristics of included studies	Allergy					
Study ID	**Aabel 2000a**					
details	Inclusion criteria: 18-50 years of age, history of birch pollen allergy, positive skin prick test for birch Exclusion criteria: other diseases (i.e. eczema, asthma), conditions causing nasal blockage, using medication of any kind, pregnant or lactating women, not willing to give up caffeine					
Description of intervention/comparator		*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	35	Sucrose globules impregnanted with Betula alba 30c. 3 day run-in period with placebo, followed by homeopathy treatment with *Betula* 30c 'one tablet daily until the allergy gets better, then stop'.			
Intervention #2						
Comparator #1 (control)	Placebo	35	Identical placebo - sucrose globules			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Comparator #3 (other)						
Co-interventions	All participants had 3 consultations with a homeopath (baseline, 2 wks, 4 wks).					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (meaure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Not specified	Nose blockage	Daily	Symptom score	The minimum possible total score each day was 0 and the maximum 51. Allergy was evaluated as sum score based on a range of different symptoms	
2	Not specified	Nose drip	Daily	Symptom score	0 = none, 3 = severe	
3	Not specified	Nose itch	Daily	Symptom score	0 = none, 3 = severe	

Characteristics of included studies	Allergy				
Study ID	**Aabel 2000a**				
4	Not specified	Nose sneeze	Daily	Symptom score	0 = none, 3 = severe
5	Not specified	Eye drip	Daily	Symptom score	0 = none, 3 = severe
6	Not specified	Eye itch	Daily	Symptom score	0 = none, 3 = severe
7	Not specified	Eye oedema	Daily	Symptom score	0 = none, 3 = severe
8	Not specified	Interior throat itch	Daily	Symptom score	0 = none, 3 = severe
9	Not specified	Exterior throat itch	Daily	Symptom score	0 = none, 3 = severe
10	Not specified	Throat mucus	Daily	Symptom score	0 = none, 3 = severe
11	Not specified	Palate itch	Daily	Symptom score	0 = none, 3 = severe
12	Not specified	Ear itch	Daily	Symptom score	0 = none, 3 = severe
13	Not specified	Skin itch	Daily	Symptom score	0 = none, 3 = severe
14	Not specified	Skin oedema	Daily	Symptom score	0 = none, 3 = severe
15	Not specified	Skin eczema	Daily	Symptom score	0 = none, 3 = severe
16	Not specified	Asthmatic breathing	Daily	Symptom score	0 = none, 3 = severe
17	Not specified	Coughing	Daily	Symptom score	0 = none, 3 = severe
18	Not specified	Use of rescue medication (antihistamines)	Daily	diary	
19	Not specified	Feeling of general energy level	Daily	0 = no energy, 3 = good energy level	
20	Not specified	Occurance of acute dieases other than allergy	Daily	diary	

Characteristics of included studies	Allergy			
Study ID	**Aabel 2000a**			
21	Not specified	Number of experimental tablets taken	Daily	diary
Method of analysis				
Statistics	A 5% significance level and statistical power of 90% were chosen. five-point difference in total sum score would be the minimum value worthy of detection. Consequently, a power analysis required the admission of 70 patients given an assumed standard deviation of 6. The mean daily symptom scores from days 1, 2 and 3 of the run-in period (RI) was calculated for all the subjects, as well as the mean scores for days 5, 6 and 7. A two-sided Wilcoxon- Mann-Whitney two-sample test was used to compare test and placebo groups.			
Population analysed	Intent-to-treat	mITT interpreted		
Missing data	Yes	2 participants in the homeopathy group and 1 in the pacebo group were excluded as they did not have allergy. 1 participant in the homeopathy group dropped out due to travelling abroad.		

Characteristics of included studies	Allergy		
Study ID	**Aabel 2000b**		
Study reference	Aabel S. No beneficial effect of isopathic prophylactic treatment for birch pollen allergy during a low-pollen season: A double-blind, placebo-controlled clinical trial of homeopathic Betula 30c. British Homeopathic Journal. 2000;89(4):169-73.		
Study design	RCT	Vials sent to statistician for coding, no mention of how the randomisation sequence was generated	
Author affiliation	Institute of General Practice and Community Medicine, Department of General Practice, Blindern, Oslo, Norway		
Source of funds	study was financed by the Research Council of Norway. The homeopathic remedy and placebo tablets were a gift from DCG, Gothenburg, Sweden.		
Declared interests of study authors	Not reported		
Setting / provider	Community setting		
Country(s) / region	Oslow, Norway		
Enrolment period	March 1996 - May 1996		
Length of intervention + follow up	4 wk prophylactic treatment + 10 day follow up		
Description of population	*N=*	*Description*	
participants	80	Birch pollen allergy	

Characteristics of included studies	Allergy					
Study ID	**Aabel 2000b**					
details	Inclusion criteria: positive skin prick test for birch Exclusion criteria: diseases of any other kind (including asthma and eczema), conditions causing nasal obstruction (like polyps, septum deviation and chronic edema), using medication of any kind, pregnant women, lactating mothers, those not willing to give up caffeine					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	40	Betula 30c - one tablet once a wk for 4 wks, thereafter one tablet when you get allergy symptoms. Wait 12 hours before taking the next. Resume tablet intake if symptoms return. If very high levels of pollen occur, you may take up to three tablets a day			
Intervention #2						
Comparator #1 (control)	Placebo	40	identical placebo - sucrose globules			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Comparator #3 (other)						
Co-interventions						
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (meaure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Allergy symptoms	daily	VAS 10-cm	higher is worse	Median score reported
2	Not specified	Number of experimental tablets	daily	patient diary		
3	Not specified	Use of rescue medication	daily	patient diary		

Characteristics of included studies	Allergy					
Study ID	**Aabel 2000b**					
4	--	--	--	--	--	--
5	--	--	--	--	--	--
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--
9	--	--	--	--	--	--
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18	--	--	--	--	--	--
19	--	--	--	--	--	--
20	--	--	--	--	--	--

Characteristics of included studies	Allergy					
Study ID	**Aabel 2000b**					
21	--	--	--	--	--	--
Method of analysis						
Statistics	Difference of 1.5 cm considered clinically relevant. A 5% significance level and 90% power was chosen. Main outcome measure was median VAS and 95% CI. Two-sided Wilcoxon-Mann-Whitney two-sample test was used to compare test and placebo groups. Chi-square test to compare frequency of persons with score >2.5.					
Population analysed	Intent-to-treat	mITT interpreted				
Missing data	Yes	Data was missing for 7/80 participants. 2 participants in the homeopathy group misunderstood instructions and did not report their symptoms. 4 in the placebo group and 1 in the homeopathy group did not return forms.				

Characteristics of included studies	Allergy	
Study ID	**Aabel 2001**	
Study reference	Aabel S. Prophylactic and acute treatment with the homeopathic medicine Betula 30c for birch pollen allergy: A double-blind, randomized, placebo-controlled study of consistency of VAS responses. British Homeopathic Journal. 2001;90(2):73-8.	
Study design	RCT	Patients from previous trials were randomised within their previous groups as strata.
Author affiliation	Institute of General Practice and Community Medicine, Department of General Practice, Blindern, Oslo, Norway	
Source of funds	study was financed by the Research Council of Norway. The homeopathic remedy and placebo tablets were a gift from DCG, Gothenburg, Sweden.	
Declared interests of study authors	Not reported	
Setting / provider	Community	
Country(s) / region	Oslow, Norway	
Enrolment period	May-97	
Length of intervention + follow up	4 wk prophylactic treatment + 10 day follow up + additional follow up if required (mean 22 days)	
Description of population	*N=*	*Description*
participants	51	Birch pollen allergy

Characteristics of included studies	Allergy					
Study ID	**Aabel 2001**					
details	As per Aabel 200a, Aabel 2000b. Participation in these previous studies was a requirement for enrolment in this study.					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	15	Betula 30c - one tablet once a wk for 4 wks, thereafter one tablet when you get allergy symptoms. Group who previously received Betula in past studies.			
Intervention #2	Non-individualised	10	Betula 30c - one tablet once a wk for 4 wks, thereafter one tablet when you get allergy symptoms. Group who previously received placebo in past studies.			
Comparator #1 (control)	Placebo	16	Identical placebo. Group who received *Betula* in past studies			
Comparator #2 (other)	Placebo	10	Identical placebo. Group who received placebo in past studies			
Comparator #3 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions						
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (meaure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Allergy symptoms	daily	VAS 10-cm	higher is worse	Both groups
2	Not specified	Number of experimental tablets	daily	patient diary		Both groups
3	Not specified	Use of rescue medication	daily	patient diary		Both groups

Characteristics of included studies	Allergy					
Study ID	**Aabel 2001**					
4	Not specified	Nose blockage	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
5	Not specified	Nose drip	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
6	Not specified	Nose itch	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
7	Not specified	Nose sneeze	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
8	Not specified	Eye drip	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
9	Not specified	Eye itch	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
10	Not specified	Eye oedema	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
11	Not specified	Interior throat itch	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
12	Not specified	Exterior throat itch	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
13	Not specified	Throat mucus	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
14	Not specified	Palate itch	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
15	Not specified	Ear itch	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
16	Not specified	Skin itch	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
17	Not specified	Skin oedema	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
18	Not specified	Skin eczema	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
19	Not specified	Asthmatic breathing	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY
20	Not specified	Coughing	Daily	Symptom score 0-3	0 = none, 3 = severe	1995 group ONLY

Characteristics of included studies	Allergy					
Study ID	**Aabel 2001**					
21	--	--	--	--	--	--
Method of analysis						
Statistics	Mean value for each participant across the whole trial period was calculated an compared with the mean value from the previous study. Scores for the 17 allergy symptom measure were transformed to VAS-values using Z-scores. Regression plots and Pearsons correlation co-efficient were used to assess consistency of responses from one trial to the next.					
Population analysed	Intent-to-treat					
Missing data	Not specified	Not reported				

Characteristics of included studies	Allergic rhinitis		
Study ID	**Kim 2005**		
Study reference	Kim LS, Riedlinger JE, Baldwin CM, Hilli L, Khalsa SV, Messer SA, Waters RF. Treatment of seasonal allergic rhinitis using homeopathic preparation of common allergens in the southwest region of the US: a randomized, controlled clinical trial. Ann Pharmacother. 2005 Apr;39(4):617-24. doi: 10.1345/aph.1E387. Epub 2005 Mar 1. PMID: 15741420.		
Study design	RCT	randomised using microsoft excel 2000 - random number generator program	
Author affiliation	Five authors affiliated with Southwest College of Naturopathic Medicine & Health Sciences, Tempe, AZ (USA), one author affiliated with Massachusetts College of Pharmacy and Health Sciences, Boston, MA and one with Southwest Borderlands, College of Nursing, Arizona State University, Tempe		
Source of funds	Southwest College of Naturopathic Medicine & Health Sciences and grant sponsorship and products provided by Dolisos America Inc.		
Declared interests of study authors	Dr. Messer holds the Dolisos Chair, which has partial underwriting from Dolisos America Inc		
Setting / provider	Community, patients enrolled from the Pheonix Metropolitan area		
Country(s) / region	Phoenix, Arizona, USA		
Enrolment period	February to May 2003		
Length of intervention + follow up	4 wks		
Description of population	*N=*	*Description*	
participants	40	Moderate to severe allergic rhinitis	

Characteristics of included studies	Allergic rhinitis					
Study ID	**Kim 2005**					
details	Inclusion criteria: moderate to severe allergic rhinitis for the last 2 years, symptoms at enrolment, ability to comply with study protocol Exclusion criteria: nonallergic rhinitis, sporadic symptoms or perennial allergic rhinitis, pregancy or lactation, smoking, medical conditions that made full participation difficult (asthma, pulmonary disorders, immunocompromised, alcohol or drug addiction), acute upper respiratory tract infection, concurrent use of other treatment for allergic rhinitis, past immunotherapy/desensitisation, previous history of homeopathy					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	18	Non-individualised homeopathy, allergens based on significant pollens reported. Allergens were prepared in 6X homeopathic dilutions and combined. Participants instructed to use 2 sprays sublingually, 3x per day after eating or drinking for 4 wks.			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	16	Spray bottle identical in colour to intervention			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	non-reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (meaure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Total symptoms	baseline, 4 wks	Rhinoconjunctivitis Quality-of-Life Questionnaire	Higher is worse. Patients respond using 7 point Likert scale (0= no impairment, 6 = extreme impairment)	
2	Primary	Activity limitation	baseline, 4 wks	Rhinoconjunctivitis Quality-of-Life Questionnaire	As above	
3	Primary	Sleep problems	baseline, 4 wks	Rhinoconjunctivitis Quality-of-Life Questionnaire	As above	

Characteristics of included studies	Allergic rhinitis				
Study ID	**Kim 2005**				
4	Primary	Non-nose/eye symptoms	baseline, 4 wks	Rhinoconjunctivitis Quality-of-Life Questionnaire	As above
5	Primary	Practical problems	baseline, 4 wks	Rhinoconjunctivitis Quality-of-Life Questionnaire	As above
6	Primary	Nose symptoms	baseline, 4 wks	Rhinoconjunctivitis Quality-of-Life Questionnaire	As above
7	Primary	Eye symptoms	baseline, 4 wks	Rhinoconjunctivitis Quality-of-Life Questionnaire	As above
8	Primary	Emotional function	baseline, 4 wks	Rhinoconjunctivitis Quality-of-Life Questionnaire	As above
9	Secondary	Activity impariment	baseline, 4 wks	Work Productivity and Activity Impairment	higher is worse. Visual analog scale from 0 to 100 (0 = no impairment, 100 = no activity/work due to allergies)
10	Secondary	Impariment at work	baseline, 4 wks	Work Productivity and Activity Impairment	As above
11	Secondary	Work time missed	baseline, 4 wks	Work Productivity and Activity Impairment	As above
12	Secondary	Overall work impairment	baseline, 4 wks	Work Productivity and Activity Impairment	As above
13	Secondary	Physical functioning	baseline, 4 wks	SF-36	
14	Secondary	Role physical	baseline, 4 wks	SF-36	
15	Secondary	Bodily pain	baseline, 4 wks	SF-36	
16	Secondary	General health	baseline, 4 wks	SF-36	
17	Secondary	Vitality	baseline, 4 wks	SF-36	Higher score indicates better quality of life. Scores range from 0 (lowest) to 100 (highest)
18	Secondary	Social functioning	baseline, 4 wks	SF-36	
19	Secondary	Role emotional	baseline, 4 wks	SF-36	
20	Secondary	Mental health	baseline, 4 wks	SF-36	

Characteristics of included studies	Allergic rhinitis			
Study ID	**Kim 2005**			
21	Secondary	Reported health transition	baseline, 4 wks	SF-36
Method of analysis				
Statistics	SPSS (version 11.0) statistical software was used for all analyses. Outcomes were reported using means and standard deviations. The estimated sample size of 20 patients per group was determined using 80% power with 2-sided (tailed) tests and α of p <0.05 to detect an actual change of 30% improvement in RQLQ total symptoms and domains. The Student's paired t-test was used to detect the within-group mean changes in RQLQ total symptoms and domains in the treatment and placebo groups from baseline to 4 wks. The changes were considered significant at p < 0.05.			
Population analysed	Intent-to-treat			
Missing data	Yes	85% participants completed study, 6 patients dropped out of the study, including 2 (10%) in the homeopathic group and 4 (20%) in the placebo group. Their discontinuation was primarily due to lack of response to treatment.		

Characteristics of included studies	Allergic rhinitis		
Study ID	**Liu 2013**		
Study reference	Liu LL, Wan KS, Cheng CF, Tsai MH, Wu YL, Wu WF. Effectiveness of MORA electronic homeopathic copies of remedies for allergic rhinitis: A short-term, randomized, placebo-controlled PILOT study. European Journal of Integrative Medicine. 2013;5(2):119-25. TCHIRB-970801		
Study design	RCT	Patients were randomly assigned by computer generated code.	
Author affiliation	2 authors affiliated with Taipei City hospital; 1 with National Yang-Ming University, Taipei; with Tamsui District public health center, New Taipei city, Taiwan; 1 with department of allergy and immunology, Taipei - Taiwan		
Source of funds	Not reported		
Declared interests of study authors	The authors declared no conflict of interest		
Setting / provider	Single centre		
Country(s) / region	Taipei, Taiwan		
Enrolment period	Not reported		
Length of intervention + follow up	4 wk intervention + 4 wk crossover		
Description of population	*N=*	*Description*	
participants	46	Immunologist diagnosed allergic rhinitis	

Characteristics of included studies	Allergic rhinitis					
Study ID	**Liu 2013**					
details	Inclusion criteria: aged 6-63 years, allergen specific IgE positive with atopic family history, confirmed ISSAC questionnaire, positive Phadiatop infant test (CAP System, Phadia Diagnostics, Uppsala, Sweden), and total nasal symptoms score (TNSS) > 6 points Exclusion criteria: patient who has previously recieved any form of immunotherapy, those treated with oral or intranasal or inhaled steroids within one mth, those with any anatomical abnormality of the sinus, those with severe disease, pregnancy or severe persistent asthma.					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	23	Non-individualised homeopathy, 4 wks. Homeopathic product was given sublingually in the morning and evening, with the capsule kept in the mouth until it dissolved. Product was produced through electromagnetic signals of the selected electronically stored parent substances and transmitted onto black sugar.			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	13	Control medication was no signal transmitted to pure black sugar.			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Comparator #3 (other)						
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (meaure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Sneezing	Baseline to 4 wks	mean difference in outcome graded on 4-point scale (0 is none, 3 is severe)	higher is better	
2	Primary	Nose running	Baseline to 4 wks	mean difference in outcome graded on 4-point scale (0 is none, 3 is severe)	higher is better	
3	Primary	Nasal	Baseline to 4 wks	mean difference in outcome graded on 4-point scale (0 is none, 3 is severe)	higher is better	

Characteristics of included studies	Allergic rhinitis					
Study ID	**Liu 2013**					
4	Primary	Itching	Baseline to 4 wks	mean difference in outcome graded on 4-point scale (0 is none, 3 is severe)	higher is better	
5	Primary	Nasal obstruction	Baseline to 4 wks	mean difference in outcome graded on 4-point scale (0 is none, 3 is severe)	higher is better	
6	Primary	Total nasal symptom score	Baseline to 4 wks	mean difference in sum of four scores above	higher is better	
7	Secondary	Serum specific IgE, IgG4 and IgG4/E ratios for *Dermatophagoides pteronyssinus*	Baseline to 4 wks	mean difference in sum of four scores above	higher is better	
8	--	--	--	--	--	--
9	--	--	--	--	--	--
10	--	--	--	--	--	--
11	--	--	--	--	--	--
12	--	--	--	--	--	--
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18	--	--	--	--	--	--
19	--	--	--	--	--	--
20	--	--	--	--	--	--

Characteristics of included studies	Allergic rhinitis					
Study ID	**Liu 2013**					
21	--	--	--	--	--	--
Method of analysis						
Statistics	Nasal symptoms before and after intervention were compared with a Mann–Whitney U-test. The non-parametric Wilcoxon signed-rank test was used to compare symptomatic score changes, and changes in specific IgE, specific IgG4, and IgG4/E ratios. SPSS ver. 13.0 was used for all statistical analysis. All tests were two-sided and a p-value < 0.05 was considered statistically significant					
Population analysed	Intent-to-treat	mITT 46 enrolled, 36 available at end of study for analysis				
Missing data	Yes	46 subjects enrolled, 36 for analysis - reason for withdrawl not specifed				

Characteristics of included studies	Seasonal rhinitis		
Study ID	**Reilly 1984**		
Study reference	Reilly D, Taylor M. A double blind placebo controlled study model for assessing homoeopathy using homoeopathic mixed grass pollens 30C in hay fever. Comm Br Homoeopath Res Grp. 1984;11:67-70. Reilly DT, Taylor MA, McSharry C, Aitchison T. Is homoeopathy a placebo response? Controlled trial of homoeopathic potency, with pollen in hayfever as model. Lancet. 1986;2(8512):881-6.		
Study design	RCT	Patients allocated random number	
Author affiliation	Glasgow Homoeopathic hospital - Univerity of Glasgow		
Source of funds	This work was supported by the Blackie Foundation Trust, the Research Council for Complementary Medicine, and the Scottish Homoeopathic Research and Education Trust.		
Declared interests of study authors	Not reported		
Setting / provider	Multicentre - two hospital clinics in glasgow		
Country(s) / region	Glasgow, Scotland		
Enrolment period	May 1 and June 18, 1984		
Length of intervention + follow up	5 wk total study period: 1 wk run-in, 2 wks intervention and 2 wks observation		
Description of population	*N=*	*Description*	
participants	158	Seasonal rhinitis	

Characteristics of included studies	Seasonal rhinitis					
Study ID	**Reilly 1984**					
details	*Inclusion criteria:* 5 years old and over,minimun 2 year history of seasonal rhinitis *Exclusion criteria:* eye involvement only, evidence of acute asthma or infection, pregnancy, lactation, risk of pregnancy, serious illness other than allergy, use of drugs other than the trial medicines					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	79	30c potency of mixed grass pollens impregnanted into lactose tablets. This was prepared from 12 species of grass most commonly associated with seasonal rhinitis in the UK.			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	79	Identically packages tablets used as placebo			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Comparator #3 (other)						
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (meaure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Overall symptom intensity	daily	100-mm VAS	higher is worse	Study was powered to detect 10mm difference
2	Secondary	sneezing	daily	Scored as 0, 1, 2, or 3	higher is worse	
3	Secondary	blocked and runny nose	daily	Scored as 0, 1, 2, or 3	higher is worse	

Characteristics of included studies	Seasonal rhinitis					
Study ID	**Reilly 1984**					
4	Secondary	watery, red irritated eyes	daily	Scored as 0, 1, 2, or 3	higher is worse	
5	Secondary	Overall symptom intensity	wk 0, 3 and 5	doctors assessment of 100-mm VAS	higher is worse	
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--
9	--	--	--	--	--	--
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19	--	--	--	--	--	--
20	--	--	--	--	--	--

Characteristics of included studies	Seasonal rhinitis					
Study ID	**Reilly 1984**					
21	--	--	--	--	--	--
Method of analysis						
Statistics	Compared groups change in mean baseline to mean final wk overall symptom scores, using 100 mm VAS. With Minitab computer software, two-sample, two-tailed t tests were used to compare differences between the groups in patient and doctor assessed VAS scores and in antihistamine intake. Chi-square tests compared the frequency of aggravations in the two groups. The two-tailed Mann-Whitney U test was applied to the skewed IgE values.					
Population analysed	Other (provide details)	Analysis population unclear, as the number of outcome returns exceeded the number of participants randomised in both arms.				
Missing data	Not specified	144/158 participants were included in the analysis				

Characteristics of included studies	Allergic rhinitis		
Study ID	**Taylor 2000**		
Study reference	Taylor MA, Reilly D, Llewellyn-Jones RH, McSharry C, Aitchison TC. Randomised controlled trial of homoeopathy versus placebo in perennial allergic rhinitis with overview of four trial series. British Medical Journal. 2000;321(7259):471-6. Taylor MA. Erratum: Randomised controlled trial of homoeopathy versus placebo in perennial allergic rhinitis with overview of four trial series (British Medical Journal (Aug. 19-26) (471-476)). British Medical Journal. 2000;321(7263):733. Taylor MA, Reilly D, Llewellyn-Jones RH, McSharry C, Aitchison TC. Randomised controlled trial of homeopathy versus placebo in perennial allergic rhinitis with overview of four trial series...including commentary by Lancaster T and Vickers A [corrected] [published erratum appears in BMJ 2001 Feb 3; 322(7281): 282]. BMJ: British Medical Journal (International Edition). 2000;321(7259):471-6.		
Study design	RCT	Restricted technique of permuted blocks of two	
Author affiliation	Glasgow Royal Infirmary, Glasgow Scotland; University of Sydney, Sydney Australia; University of Glasgow, Glasgow Scotland.		
Source of funds	Fondation Française pour la Recherche en Homeo-pathie, Blackie Foundation Trust, British Homoeopathic Association, and Scottish Homoeopathic Research and Education Trust. The project was initially part of a research fellowship created by the Research Council for Complementary Medicine in partner- ship with the Medical Research Council and the King's Fund.		
Declared interests of study authors	MAT's salary was partly paid by the Blackie Foundation Trust, British Homoeopathic Association, and Scottish Homoeopathic Research and Education Trust administered by Glasgow University. She was reimbursed for attending a symposium organised by the Blackie Foundation Trust. DR began this research programme before using homoeopathy or developing education. He uses homoeopathy in clinical care.-		
Setting / provider	Multicentre - four general practices and a hospital outpatient department		
Country(s) / region	London, UK		
Enrolment period	6 wks from the middle of Feburary, year not specified		
Length of intervention + follow up	2 wk tun in period, 4 wk intervention, no further follow up		
Description of population	*N=*	*Description*	
participants	51	Perennial allergic rhinitis	

Characteristics of included studies	Allergic rhinitis						
Study ID	**Taylor 2000**						
details	Inclusion criteria: age >16 years, atopic (reactive to inhaled allergens with positive skin test results), more than 1 year history of perennial rhinitis Exclusion criteria: deterioration during grass pollen season, nasal abnormalities causing obstruction, previous homoeopathic immunotherapy, allergen avoidance in past 6 wks, away from usual environment for more than 1 wk during trial, respiratory infection, severe concomitant disease, pregnant or breastfeeding, oral or parenteral steroids in past 6 mths, conventional desensitisation in past 3 mths, long acting antihistamines in past 4 wks, topical steroids, vasoconstrictors or antihistamines in past 2 wks						
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*				
Intervention #1	Individualised	24	Lactose-sucrose globules impregnated with 30c homeopathic dilution - the principal allergen was selected on the basis of the largest skin test weal concordant with the allergy history. The phials consistuted a split single dose that was to be taken equally spaced over 24 hours.				
Intervention #2							
Comparator #1 (control)	Placebo	27	Identical placebo without the allergen.				
Comparator #2 (other)	--	--	--				
Comparator #3 (other)	--	--	--				
Comparator #3 (other)							
Co-interventions	None reported						
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis					
Outcomes (meaure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*	
1	Primary	nasal obstruction	each morning and evening	Youlten nasal inspiratory peak flow meter	higher is worse		
2	Not specified	how symptoms had interferred with sleep	each night	0 to 4 interger scale	higher is worse		
3	Primary	overall VAS scale score	daily	0-100 mm VAS	higher is worse		

Characteristics of included studies	Allergic rhinitis					
Study ID	**Taylor 2000**					
4	Not specified	medication use	any use of	patient diary	--	
5	Not specified	Adverse events	any occurred	patient diary	--	
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--
9	--	--	--	--	--	--
10	--	--	--	--	--	--
11	--	--	--	--	--	--
12	--	--	--	--	--	--
13	--	--	--	--	--	--
14	--	--	--	--	--	--
15	--	--	--	--	--	--
16	--	--	--	--	--	--
17	--	--	--	--	--	--
18	--	--	--	--	--	--
19	--	--	--	--	--	--
20	--	--	--	--	--	--

Characteristics of included studies	Allergic rhinitis					
Study ID	**Taylor 2000**					
21	--	--	--	--	--	--
Method of analysis						
Statistics	Variables with normal distributions (nasal inspiratory peak flow and visual analogue scale) were analysed by using two tailed, two sample t tests and confidence intervals. X^2 tests were applied to categorical compari-sons and proportions, but if any cell in a contingency table was less than 5, Fisher's exact test was used					
Population analysed	Intent-to-treat	ITT analysis specified				
Missing data	No	1/51 participants lost to follow up. This participant was allocated to the homoeopathy arm				

Characteristics of included studies	Allergy		
Study ID	**Naidoo 2013**		
Study reference	Naidoo P, Pellow J. A randomized placebo-controlled pilot study of Cat saliva 9cH and Histaminum 9cH in cat allergic adults. Homeopathy: the Journal of the Faculty of Homeopathy. 2013;102(2):123-9.		
Study design	RCT	Simple random sampling	
Author affiliation	Department of homeopathy, university of Johannesburg		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Single centre - homeopathic health training centre		
Country(s) / region	Johannesburg, South Africa		
Enrolment period	not specified		
Length of intervention + follow up	4 wk intervention, no follow up reported		
Description of population	*N=*	*Description*	
participants	30	Positive cat allergy skin prick test	

Characteristics of included studies	Allergy					
Study ID	**Naidoo 2013**					
details	Inclusion criteria Aged 18-45, positive skin prick test to cat allergy, living with a cat for a period of 6 mths or more and be suffering from allergy like symptoms when in the presence of a cat Exclusion criteria Pregnant or lactating, using any other medication of intervention for allergy, immunocompromised					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	15	Cat Saliva 9cH and *Histaminum* 9cH lactose tablet. Participants were instructed to dissolve two tablets under the tongue twice daily, morning and night.			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	15	The placebo was manufactured to be identical in taste and appearance to the homoeopathic product.			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Comparator #3 (other)						
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (meaure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Wheal diameter	wk 0, wk 4	Skin prick test	Scale 1-4, higher score is worse	
2	Primary	Flare reaction	wk 0, wk 5	Skin prick test	Scale 1-4, higher score is worse	
3	Primary	Itchiness	wk 0, wk 6	Skin prick test	Scale 1-4, higher score is worse	

Characteristics of included studies	Allergy					
Study ID	**Naidoo 2013**					
4	--	--	--	--	--	--
5	--	--	--	--	--	--
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--
9	--	--	--	--	--	--
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12	--	--	--	--	--	--
13	--	--	--	--	--	--
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15	--	--	--	--	--	--
16	--	--	--	--	--	--
17	--	--	--	--	--	--
18	--	--	--	--	--	--
19	--	--	--	--	--	--
20	--	--	--	--	--	--

Characteristics of included studies	Allergy					
Study ID	**Naidoo 2013**					
21	--	--	--	--	--	--
Method of analysis						
Statistics	Data from each participant was statistically analysed using non-parametric test, due to small sample size. Comparison between groups done using Mann-Whitney Test.					
Population analysed	Intent-to-treat					
Missing data	No	No drop out reported, all randomised participants were analysed				

Characteristics of included studies	Hay fever		
Study ID	**Wiesenauer 1995**		
Study reference	Wiesenauer M, Lüdtke R. The treatment of pollinosis with Galphimia glauca D4 - a randomized placebo-controlled double-blind clinical trial -. Phytomedicine. 1995 Jul;2(1):3-6. doi: 10.1016/S0944-7113(11)80041-3. PMID: 23196093.		
Study design	RCT	Stratified randomisation	
Author affiliation	University of Gottingen, Germany		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Multicentre - recruited from 27 physicians		
Country(s) / region	Germany		
Enrolment period	Spring to Autumn 1987		
Length of intervention + follow up	4 wks		
Description of population	*N=*	*Description*	
participants	164	Hay fever (pollinosis)	

Characteristics of included studies	Hay fever					
Study ID	**Wiesenauer 1995**					
details	*Inclusion criteria:* Under medical treatment for pollinosis for at least two years *Exclusion criteria:* Patients treated for other diseases with corticosteroids or antihistamines drugs					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised		*Galphimia glauca* D4. The choice of medication frequency was left to the homoeopaths.			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo		Identical sucrose tablets in identical bottles. No difference in appearance or taste.			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Comparator #3 (other)						
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (meaure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Not specified	Therapy success	every 2 wks	Rating scale 1. symptom-free, i.e. the patient showed no symptoms at all 2. obvious relief, i.e. noticeable and soothing relief		
2	Not specified	patients subjective statements on therapy	every 2 wks	physicians record of patient statement		
3	Not specified	Compliance	every 2 wks	physicians record		

Characteristics of included studies	Hay fever					
Study ID	**Wiesenauer 1995**					
4	Not specified	additional drug intake	every 2 wks	physicians record		
5	Not specified	adverse effects	every 2 wks	physicians record		
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--
9	--	--	--	--	--	--
10	--	--	--	--	--	--
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20	--	--	--	--	--	--

Characteristics of included studies	Hay fever					
Study ID	**Wiesenauer 1995**					
21	--	--	--	--	--	--
Method of analysis						
Statistics	Statistical evaluation was done with Kruskal and Wallis' rank test using the statistical software package StatXactTurbo®. With respect to the four-level rating scale authors included a correction for ties. Significance assumed at a = 5%					
Population analysed	Per protocol	Participants who took additional antiphlogistic, antiinflammatory or antiallergic drugs were excluded from the analysis.				
Missing data	Yes	32 cases (18 verum, 14 placebo) excluded from study because of incomplete documentation, self-medication or additional hayfever medication administered by physicians during study				

Characteristics of included studies	Atopic dermatitis		
Study ID	**Carello 2017**		
Study reference	Carello R, Ricottini L, Miranda V, Panei P, Rocchi L, Arcieri R, Galli E. Long-term treatment with low-dose medicine in chronic childhood eczema: a double-blind two-stage randomized control trial. Ital J Pediatr. 2017 Sep 6;43(1):78. doi: 10.1186/s13052-017-0393-5. PMID: 28874171; PMCID: PMC5585968.		
Study design	RCT	crossover trial	Computer randomisation, block size of 16
Author affiliation	Department of Pediatric Allergy, San Pietro Hospital Fatebenefratelli, Rome, Italy. Clinical Research Unit, Milan, Italy.		
Source of funds	Study was funded by Guna S.p.a., Milan, Italy		
Declared interests of study authors	VM works for the pharmaceutical company Guna S.p.a., Milan, Italy. LR is an external coordinator of the Clinical Research Unit, Guna S.p.a.,		
Setting / provider	Single centre - hospital department of paediatric allergy		
Country(s) / region	Italy		
Enrolment period	February 2010 to July 2013		
Length of intervention + follow up	First stage 8 mths, 6 mths follow up. Second stage 8 mths, 6 mth follow up.		
Description of population	*N=*	*Description*	
participants	80	Children, aged 18 mths to 16 years with mild/moderate chronic eczema, diagnosed according to Hanifin and Rajka criteria	
details	*Inclusion criteria:* Children affected by chronic mild/moderate eczema (SCORAD index: <6 – <40), with at least 4 relapses per year, and with onset of skin lesions at least 6 mths before the study (all children were in an acute phase of the disease upon enrolment); children with IgE-mediated eczema (i.e., children who tested positive to specific in vivo and/or in vitro tests, and children with non-IgE-mediated eczema (negative to specific in vivo and/or in vitro tests) *Exclusion criteria:* Systemic treatment with corticosteroids and antihistamines, with topical calcineurin inhibitors (tacrolimus and/or pimecrolimus) or with specific immunotherapy in the three mths before the study; and severe eczema associated systemic disorder		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Atopic dermatitis					
Study ID	**Carello 2017**					
Intervention #1	Non-individualised	40	Galium-Heel®, a low-dose multicomponent medicine based upon natural substances: Guna-Interleukin 12 and Guna-Interferon-γ. Administered orally, twice a day for 2 mths on/1 mth off for 8 mths.			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	40	Placebo: hydro-alcoholic solution 30% without active ingredients. Same administration pattern as the intervention arm.			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)						
Co-interventions	Conventional therapy (topical steroids, oral antibiotics and antihistamines) when necessary to alleviate symptoms.					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Disease severity	3,6,8,14 mths	Scoring Atopic Dermatitis (SCORAD) index	Higher is worse	
2	Secondary	Disease free interval	3,6,8,14 mths	Not specified	Higher is better	
3	Secondary	Treatment safety	3,6,8,14 mths		-	
4	Secondary	Treatment tolerability	3,6,8,14 mths		-	
5	Secondary	Skin prick test for inhalant and food allergens	3,6,8,14 mths	Skin prick test for inhalant and food allergens	-	
6	Secondary	Skin prick-by-prick	3,6,8,14 mths	Skin prick test	-	
7	Secondary	Inflammatory biomarkers	3,6,8,14 mths	Total and specific IgE assessment and serum cytokine level of IL-4, IL-10, IL-12, IL-13, IFN-γ		
8	Secondary	Itching	not specified	Clinical diary		

Characteristics of included studies	Atopic dermatitis			
Study ID	**Carello 2017**			
8	Secondary	Sleep disturbances	not specified	Clinical diary
8	Secondary	Use of rescue medication	not specified	Clinical diary
Method of analysis				
Statistics	The data were analysed with SPSS 22 and OpenEpi 3.02 software packages. Categorical variables are presented as absolute and percent frequencies, and quantitative variables are showed as means ± standard deviations. The data were analysed separately from T0 to T3, from T3 to T6, from T6 to T8, and from T8 to T14 to assess the efficacy of the treatment in reducing the SCORAD index. Two groups were compared at difference times to evaluate the relative effectiveness of the two treatments. Probability (odds ratio) of disease-free interval between study groups calculated using person/time to normalise the number of subjects in each group.			
Population analysed	Intent-to-treat	Performed an intention-to-treat analysis and per-protocol analysis		
Missing data	Yes	During stage 1: 6 discontinued intervention in placebo group and 8 in intervention group		

Characteristics of included studies	Atopic dermatitis		
Study ID	**Dey 2022**		
Study reference	Dey S, Shaikh AR, Saha S, Agrawal E, Gautam AK, Karuppusamy A, Sadhukhan S, Dutta S, Ali SS, Basu A, Koley M, Saha S. Efficacy of Individualized Homeopathic Medicines in the Treatment of Atopic Dermatitis in Adults: A Double-Blind, Randomized, Placebo-Controlled, Preliminary Trial. Complement Med Res. 2022;29(1):17-26. English. doi: 10.1159/000516026. Epub 2021 Apr 15. PMID: 33857943		
Study design	RCT	Permuted block randomization method was used to generate a random sequence	
Author affiliation	Homoeopathic Medical College and Hospital, Government of West Bengal, India The Calcutta Homoeopathic Medical College and Hospital, India		
Source of funds	Authors received no funding for the project. Institutional infrastructure was provided by D.N. De Homoeopathic Medical College and Hospital, Kolkata, West Bengal		
Declared interests of study authors	The authors have no conflict of interest to declare		
Setting / provider	Single centre - dermatology outpatient department of D.N. De Homeopathic Medical College and Hospital, Government of West Bengal, India		
Country(s) / region	West Bengal, India		
Enrolment period	March 2018 - December 2018		
Length of intervention + follow up	3 mth intervention, no further follow up reported		
Description of population	*N=*	*Description*	
participants	60	Newly diagnosed atopic dermatitis	
details	*Inclusion criteria:* Newly diagnosed atopic dermatitis as per UK diagnostic criteria and patient orientated scouring of AD (PO-SCORAD) more than 10 age 18–65 years, both sexes, literate patients, and providing written informed consent to participate in the trial *Exclusion criteria:* patients who were too sick for consultation, diagnosed cases of unstable psychiatric illness affecting QoL, uncontrolled or life-threatening illness affecting QoL or any organ failure, substance abuse and/or dependence, pregnant and lactating women, and patients undergoing homeopathic treatment for any chronic disease within the last 6 mths		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Atopic dermatitis					
Study ID	**Dey 2022**					
Intervention #1	Individualised	30	4-6 globules, orally on a clean tongue with an empty stomach, dosage and repetition depending upon individuals requirements of the cases. Intervention duration was 3 mths. Homeopathic medicinal products were permitted to change throughout the course of the trial.			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	30	Identical placebo, also administered as 4-6 globules moistened with rectified spirit, to be taken orally on a clean tongue, with empty stomach; dosage and repetition dependent on requirements of individual cases.			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)						
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Disease severity	mthly for 3 consecutive mths	PO-SCORAD	higher is worse	Conducted by a blinded, conventionally trained physician
2	Secondary	Quality of life	mthly for 3 consecutive mths	Dermatological life quality index score	higher is better	
3	Secondary	Burden of disease	mthly for 3 consecutive mths	AD burden scale for adults	higher is worse	
4	--	--	--	--	--	--
5	--	--	--	--	--	--
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--

Characteristics of included studies	Atopic dermatitis					
Study ID	**Dey 2022**					
8	--	--	--	--	--	--
8	--	--	--	--	--	--
Method of analysis						
Statistics	Baseline descriptive data (categorical and continuous – age, sex, body mass index, residence, socioeconomic status, and positive family history of AD) were presented in terms of absolute values, percentages, mean, standard deviations (SD), and confidence intervals (CI). Baseline differences were adjusted by analysis of covariance (ANCOVA) models. Parametric tests were used as inferential statistics. Group differences (independent observations) were tested at baseline (to check comparability) and every mth up to 3 mths (to check efficacy) by $\chi 2$ tests and unpaired t tests. p values were set at < 0.05 two-tailed as statistically significant. All analyses were carried out in SPSS® IBM® version 20 for Windows.					
Population analysed	Intent-to-treat	Analysis was carried out on an intention-to-treat approach.				
Missing data	Yes	9/60 participants did not complete the follow up period. Missing values were replaced by the last observation carried forward method				

Characteristics of included studies	Atopic dermatitis		
Study ID	**Vickers 2000**		
Study reference	Vickers A. Evaluation of specific and non-specific effects in homeopathy: Feasibility study for a randomised trial. British Homeopathic Journal. 2000;89(SUPPL. 1):S48-S9. Fisher P, McCarney R, Hasford C, Vickers A. Evaluation of specific and non-specific effects in homeopathy: feasibility study for a randomised trial. Homeopathy. 2006 Oct;95(4):215-22. doi: 10.1016/j.homp.2006.07.006. PMID: 17015192.		
Study design	RCT	Randomisation in permuted blocks of 8 and 12 is by a computer system designed to ensure allocation concealment	
Author affiliation	Royal London Homoeopathic Hospital, Great Ormond Street, London		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Single centre outpatient clinic- Royal London Homeopathic Hospital		
Country(s) / region	London, United Kingdom		
Enrolment period	The first participant entered the study in March 1999, the last participant completed the study in November 2001.		
Length of intervention + follow up	12 wks		
Description of population	*N=*	*Description*	
participants	75	Adult patients with dermatitis	
details	*Inclusion criteria:* Planned treatment for dermatitis at the RLHH; Age 18–65 *Exclusion criteria:* Pregnancy or intended pregnancy; Malignant disease; Other serious pathology; Current use of systemic corticosteroids		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Atopic dermatitis					
Study ID	**Vickers 2000**					
Intervention #1	Individualised	22	Fast track open verum homeopathy (patients receiving unblinded homeopathic treatment). Participants saw a homeopath, treatment was entirely at the discretion of the homeopath. Follow up appointment after 6 wks, where treatment could be adjusted.			
Intervention #2	Individualised	22	Fast track double-blind verum homeopathy (patients receiving blinded homeopathic treatment). Participants saw a homeopath, treatment was entirely at the discretion of the homeopath. Follow up appointment after 6 wks, where treatment could be adjusted.			
Comparator #1 (control)	Placebo	16	Fast track double-blind placebo homeopathy. Placebo consisted of lactose pills impregnated with 95% pharmaceutical ethanol. They were identical in appearance, odour and taste to homeopathy.			
Comparator #2 (other)	Inactive control	15	Waiting list control			
Comparator #3 (other)						
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Overall symptom severity	Daily for 13 wks	100 mm VAS	higher is worse	
2	Secondary	Sleep	Daily for 13 wks	10 point NRS	higher is worse	
3	Secondary	Itching	Daily for 13 wks	10 point NRS	higher is worse	
4	Secondary	Skin condition	Daily for 13 wks	10 point NRS	higher is worse	
5	Secondary	Frequency of steroid ointment use	Daily for 13 wks	5-point Likert scale	higher is worse	
6	Secondary	Quality of life	Daily for 13 wks	Dermatology Life Quality Index		
7	--	--	--	--	--	--
8	--	--	--	--	--	--

Characteristics of included studies	Atopic dermatitis					
Study ID	**Vickers 2000**					
8	--	--	--	--	--	--
8	--	--	--	--	--	--
Method of analysis						
Statistics	Post-treatment outcomes were entered into a linear regression model with baseline score as a covariate. Treatment allocation was entered as dummy variables corresponding to the three presumed aspects of homeopathic effect: seeing a homeopath, receiving a homeopathic medicine, knowing that treatment is being received. Thus the groups were coded as follows: waiting list control (0,0,0); blinded placebo (1,0,0); blinded verum (1,1,0); open homeopathy (1,1,1).					
Population analysed	Intent-to-treat	Analyses were performed on 'intention to treat' basis and corrected for baseline differences and multiple comparisons.				
Missing data	Yes	14/75 participants did not return outcome diary. No reasons provided				

Characteristics of included studies	Otitis media with effusion		
Study ID	**Harrison 1999**		
Study reference	Harrison H, Fixsen A, Vickers A. A randomized comparison of homoeopathic and standard care for the treatment of glue ear in children. Complementary Therapies in Medicine. 1999;7(3):132-5.		
Study design	quasi RCT	The study was conducted in two locations. In Swindon, randomisation was done on an alternate basis. In the Isle of Wright, sealed envelopes were used. No further details were provided.	
Author affiliation	One of the authors was affiliated with the research council for complementary medicine, London. The other authors had no specific affiliations		
Source of funds	The paper was funded by the research council for complementary medicine		
Declared interests of study authors	Not reported		
Setting / provider	General practices in 2 locations in England		
Country(s) / region	England, UK		
Enrolment period	Not reported		
Length of intervention + follow up	12 mth intervention and follow up		
Description of population	*N=*	*Description*	
participants	33	Children with otitis media with effusion	
details	Inclusion criteria: A positive diagnosis of otitis media with effusion by the patient's GP; hearing loss >20dBHL; an abnormal tympanogram (i.e. flat with absent reflexes) and patients in the age range 18 mths to 8 years of age. Exclusion criteria: A congenital abnormality affecting the ears or throat; Down's syndrome or other substantial abnormalities; a history of surgical interventions (e.g. adenoidectomy, tonsillectomy or grommet insertion) or tympanic membrane disease.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Otitis media with effusion					
Study ID	**Harrison 1999**					
Intervention #1	Individualised	17	Participants received an initial consultation with a homeopath in addition to mthly follow ups for 12 mths. They were prescribed individualised homeopathy based on treating the totality of symptoms			
Intervention #2	--	--	--			
Comparator #1 (control)	Inactive control	16	Standard care, which involved a 'watch and wait' policy. Participants did not have consultations with the homeopath.			
Comparator #2 (other)	--	--	--	--	--	--
Comparator #3 (other)	--	--	--	--	--	--
Co-interventions	Standard care. Both groups were able to access GP visits, specialists referrals and antibiotics as needed					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Control (no intervention)	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Hearing loss	Baseline, 3, 6, 9 and 12 mths	Audiometric measurements	Presented as a binary outcomes at 12 mths (<20bB or >20dB of hearing loss)	
2	Primary	Tympanometry changes	Baseline, 3, 6, 9 and 12 mths	Tympanometry measurements	Presented as categorical outcomes at 12 mths (normal, fluid or flat)	
3	Secondary	Antibiotic use	Baseline, 3, 6, 9 and 12 mths	Number of courses of antibiotics taken	Frequency of antibiotic use presented as a binary outcomes at 12 mths (1 or more, or none)	

Characteristics of included studies	Otitis media with effusion					
Study ID	**Harrison 1999**					
4	Secondary	Referrals to specialists	Baseline, 3, 6, 9 and 12 mths	Number of referrals for myringotomy/ grommets and speech therapy	Frequency of referrals presented as binary outcomes at 12 mths (myringotomy/grommets or speech therapy)	
5	--	--	--	--	--	--
6	--	--	--	--	--	--
Method of analysis						
Statistics	Difference between groups calculated using chi squared tests. Fisher's test used for significance.					
Population analysed	Intent-to-treat	Presumed ITT analysis				
Missing data	Yes	2/33 participants had missing data				

Characteristics of included studies	Otitis media		
Study ID	**Jacobs 2001**		
Study reference	Jacobs J, Springer DA, Crothers D. Homeopathic treatment of acute otitis media in children: A preliminary randomized placebo-controlled trial. Pediatric Infectious Disease Journal. 2001;20(2):177-83. Jacobs J, Springer DA, Crothers D, Walach H. Homeopathic treatment of acute otitis media: Hoping for the best. [German]. Forschende Komplementarmedizin und Klassische Naturheilkunde. 2001;8(5):315-6. Jacobs J, Springer DA, Crothers D. Homeopathic treatment of otitis media in children: a preliminary randomized controlled trial with placebo. Homeopatia mex. 2002;71(618):109-21.		
Study design	RCT	Study medications were randomised into coded bottles by a homeopathic pharmacist. Coded bottles were randomised to contain either active medication or placebo by random number generator and pattern blocks of 4 and 6. Participants were given the next bottle in the sequence.	
Author affiliation	Authors were affiliated with the University of Washington and Evergreen Centre for Homeopathic Medicine, Washington, USA.		
Source of funds	The study was funded by the Standard Homeopathic Company		
Declared interests of study authors	Not reported		
Setting / provider	Outpatient clinic		
Country(s) / region	Seattle, Washington, USA		
Enrolment period	January 1996 to January 1997		
Length of intervention + follow up	6 wk follow up		
Description of population	*N=*	*Description*	
participants	75	Children with acute otitis media	
details	Inclusion criteria: Aged 18mths to 6 years, diagnosis of acute otitis media (middle ear effusion with one of both of the ear pain characterised as moderate or severe, and fever >38C degrees. Exclusion criteria: Patients with a history of ear pain for >36 h or those who had received antibiotics within the past wk or homeopathic medications within the previous 72 hrs, previous tonsillectomy, adenoidectomy or tympanostomy tubes as well as those with a perforated tympanic membrane and/or a discharge from the ear. Children on concurrent medication for another acute or chronic illness, those with a cleft palate or Down's syndrome.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Otitis media					
Study ID	**Jacobs 2001**					
Intervention #1	Individualised	36	Participants met with a homeopath and were prescribed a homeopathic treatment. Treatment was administered orally, 3-5 pellets 3 times daily for 5 days or until improvement occurred.			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	39	Participants met with a homeopath and received a placebo that was administered orally, 3-5 pellets 3 times daily for 5 days or until improvement occurred			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Treatment failure	After 5 days, 2 wks and 6 wks	Proportion with treatment failure	ear pain and/or a fever of greater than 38C orally at any time after the first 48 h of treatment; or severe ear pain (crying from pain)and/or a fever of greater than 39C orally	
2	Secondary	Symptom severity	Recorded 3 times daily for the first 3 days (parent reported), 2 & 6 wks	Mean diary symptom score over time	Daily symptom diaries, included information on pain, fever, irritability, appetite, energy level, sleep, concurrent upper respiratory tract symptoms and number of doses of study medications given Higher is worse	
3	Secondary	Middle ear effusion	2 and 6 wks post treatment	Tympanogram	Reported as the number of participants with middle ear effusion.	

Characteristics of included studies	Otitis media					
Study ID	**Jacobs 2001**					
4	--	--	--	--	--	--
5	--	--	--	--	--	--
6	--	--	--	--	--	--
Method of analysis						
Statistics	The Yates corrected chi square statistic of two-by-two tables was used to compare the proportion of treatment failures between the two groups at 5 days, as well as treatment failures and the presence of middle ear effusion at the 2- and 6-wk follow-up. Relative risks with confidence intervals were also calculated for these results. Student's t test (two tailed) was used to compare the mean symptom scores between the two groups as reported in the parent diaries at various time points					
Population analysed	Intent-to-treat	ITT analysis performed				
Missing data	Yes	3/75 participants had missing data				

Characteristics of included studies	Otitis media with effusion		
Study ID	**Pedrero-Escalas 2016**		
Study reference	Pedrero-Escalas MF, Jimenez-Antolin J, Lassaletta L, Diaz-Saez G, Gavilan J. Hospital clinical trial: Homeopathy (Agraphis nutans 5CH, Thuya occidentalis 5CH, Kalium muriaticum 9CH and Arsenicum iodatum 9CH) as adjuvant, in children with otitis media with effusion. International Journal of Pediatric Otorhinolaryngology. 2016;88:217-23. ISRCTN11416813; EudraCT 2011-006086-17		
Study design	RCT	Treatment assignment was set up with a permuted-block randomization algorithm and a masking plan was followed to guarantee the double-blindness	
Author affiliation	Authors were affiliated with hospitals in Spain and Boiron, Spain		
Source of funds	The study was funded by Boiron Laboratories		
Declared interests of study authors	Not reported		
Setting / provider	Outpatient clinic		
Country(s) / region	Spain		
Enrolment period	1 January 2013 to 31 December 2013		
Length of intervention + follow up	3 mth follow up		
Description of population	*N=*	*Description*	
participants	96	Children with otitis media with effusion (OME)	
details	Inclusion criteria: Aged from 2 mths to 12 years with otitis media with effusion, diagnosed by PNO examination. Exclusion criteria: Neonatal screening fail, receptive language disorder, neurosensorial hearing loss, autism, craniofacial abnormalities, Down Syndrome, middle or internal ear malformation, ciliary motility disorders, cholesteatoma, acute mastoiditis, acute otitis media, recent vaccination (less of 30 days), obstructive sleep apnoea, tympanic perforation or Tympanostomy tubes, adenoidectomy, lactose or glucose intolerance, treating asthma, corticoid, antihistamine or mucolytics therapy.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Otitis media with effusion					
Study ID	**Pedrero-Escalas 2016**					
Intervention #1	Non-individualised	45	Participants received aerosol therapy consisting of one session every 24hrs for 20 days of 1 vial of ambroxol hydrochloride, 1 vial of budesonide and 2cc of physiological saline. Participants also received homeopathic treatment A (Agraphis nutans 5CH and Thuya Occidentalis 5CH) with a dosage of 5 granules of each, once a day, preferably in the evening and homeopathic treatment B (Kalium muriaticum 9CH and Arsenicum iodatum 9CH) with a dosage of 5 granules, twice a day			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	50	Participants received the same therapeutic drugs scheme with aerosol therapy and placebo treatment instead of the homeopathy treatment			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Both groups received aerosol therapy with corticosteroids and mucolytics					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Recovery from OME	Baseline, 45 days, end of treatment (90 days)	Pneumatic otoscopy (PNO)	Reported as the number who had recovered from OME (PNO changed from negative to positive between visit 1 and 3)	
2	Primary	Infection frequency	Baseline, 45 days, end of treatment (90 days)	Recurrence of OME	Reported as the number who had a recurrence of OME (PNO changed from positive to negative between visit 2 and 3)	
3	Secondary	Adverse events	At 45 days, 90 days, 120 days post intervention	Number of adverse events	Higher is worse	

Characteristics of included studies	Otitis media with effusion				
Study ID	**Pedrero-Escalas 2016**				
4	Secondary	Otological complications	Baseline, 45 days, end of treatment (90 days)	Frequency of acute otitis media	Higher is worse
5	Secondary	Otological complications	45 days end of treatment (90 days)	Frequency of eardrum perforation	Higher is worse
6	Secondary	Otological complications	45 days end of treatment (90 days)	Frequency of mastoiditis	Higher is worse
Method of analysis					
Statistics	Differences between the intervention groups were compared through the Student-T test in the case of quantitative variables that followed a normal distribution, or a Mann Whitney U test if they did not. Categorical variables were compared using the Chi-Square test or Fisher's Exact test. In the case of variables that were not homogeneous at baseline between research groups, univariate and multivariate logistic regression models were performed.				
Population analysed	Intent-to-treat	ITT analysis performed			
Missing data	Yes	10/96 participants had missing data			

Characteristics of included studies	Otitis media		
Study ID	**Sinha 2012**		
Study reference	Sinha MN, Siddiqui VA, Nayak C, Singh V, Dixit R, Dewan D, et al. Randomized controlled pilot study to compare Homeopathy and Conventional therapy in Acute Otitis Media. Homeopathy: the Journal of the Faculty of Homeopathy. 2012;101(1):5-12.		
Study design	RCT	Computer generated random numbers	
Author affiliation	Authors were affiliated with homeopathic research centres in India		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Outpatient clinic		
Country(s) / region	Jaipur, India		
Enrolment period	May 2009 to April 2010		
Length of intervention + follow up	21 day intervention		
Description of population	*N=*	*Description*	
participants	81	Children with acute otitis media	
details	Inclusion criteria: Children of both sexes, between 2 and 6 years of age. Earache of not more than 36 h duration. Tympanic membrane bulging with loss of landmarks. Exclusion criteria: Patients having any discharge or history of discharge from ear; history of convulsions; subperiosteal abscess of mastoid; grossly deviated nasal septum; suspected enlarged adenoids (persistent nasal discharge, snoring, history of tonsillar hypertrophy); Otitis Media with effusion (OME); on antibiotics in the past 7 days or on steroid therapy; suffering from any systemic disease.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Otitis media				
Study ID	**Sinha 2012**				
Intervention #1	Individualised	40	Participants were prescribed a treatment based on the totality of symptoms. Treatment was started with 0/1 (LM potency) and followed by next higher potency in ascending manner as required. Medicine was repeated 2 - 6 hourly depending on severity of symptoms. Both groups were treated with antibiotics if less than 50% improvement was observed in first 3 days of treatment		
Intervention #2	--	--	--		
Comparator #1 (control)	Active control	41	Participants were observed for the first 3 days, with management consisting of symptomatic relief using analgesic, anti-inflammatory and antipyretics. Both groups were treated with antibiotics if less than 50% improvement was observed in first 3 days of treatment		
Comparator #2 (other)	--	--	--		
Comparator #3 (other)	--	--	--		
Co-interventions	Both groups were treated with antibiotics if less than 50% improvement was observed in first 3 days of treatment				
Is comparator clearly inactive?	No	Comparison=other			Active control
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Severity	Baseline, 3rd, 7th 10th and 21st day (end of treatment)	Acute otitis media severity of symptoms scale (AOM-SOS)	Range: 0 - 22 Higher is worse
2	Primary	Tympanic membrane appearance	Baseline, 3rd, 7th 10th and 21st day (end of treatment)	Tympanic membrane examination scale	Range: 0 - 8 Higher is worse
3	--	--	--	--	--

Characteristics of included studies	Otitis media				
Study ID	**Sinha 2012**				
4	--	--	--	--	--
5	--	--	--	--	--
6	--	--	--	--	--
Method of analysis					
Statistics	Analysis was performed on demographic data, symptom score and treatment outcome by the Mann-Whitney test, independent 't' test and Chi-square test. Analysis was by Intention to Treat: missing data of patients withdrawn due to non-reporting, were replaced on the last observation carried forward (LOCF) principle				
Population analysed	Intent-to-treat	ITT analysis performed			
Missing data	Yes	3/81 patients had missing data			

Characteristics of included studies	Otitis media		
Study ID	**Taylor 2011**		
Study reference	Taylor JA, Jacobs J. Homeopathic ear drops as an adjunct to standard therapy in children with acute otitis media. Homeopathy: the Journal of the Faculty of Homeopathy. 2011;100(3):109-15. NCT00622518		
Study design	RCT	Computer generated randomisation schedule. Randomization was stratified by antibiotic treatment plan (immediate or delayed therapy) and in blocks of 4	
Author affiliation	Authors were affiliated with the university of Washington, Seattle, USA		
Source of funds	Study was funded by Standard Homeopathic Company, California, LA		
Declared interests of study authors	2nd author had been a paid consultant for the study sponsor. First author declared no conflicts		
Setting / provider	Outpatient clinic		
Country(s) / region	Seattle, Washington, USA		
Enrolment period	Not reported		
Length of intervention + follow up	Five day intervention, plus additional follow up after 12-15 days		
Description of population	*N=*	*Description*	
participants	119	Children with acute otitis media	
details	Inclusion criteria: Children 6 mths - 11 years old diagnosed with AOM, children whose tympanic membrane(s) was distinctly abnormal and who had significant discomfort related to AOM, met the severity requirements of the study. Exclusion criteria: Children with a chronic medical condition, those who had received antibiotics within the previous 2 days, had a diagnosis of AOM during the preceding 30 days, or who had a perforated tympanic membrane.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Otitis media					
Study ID	**Taylor 2011**					
Intervention #1	Non-individualised	59	Participants were prescribed homeopathic ear drops "Hyland's Earache Drops", made of a combination of 6 homeopathic remedies at 30c potency. 3-4 drops up to 3 times daily or as needed for a maximum of 5 days			
Intervention #2	--	--	--			
Comparator #1 (control)	Inactive control	60	Participants received no intervention. Standard care was provided to both groups			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Standard care consisting of antibiotics, as well as treatments for otalgia such as acetaminophen, ibuprofen, or topical benzocaine ear drops					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Control (no intervention)	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Secondary	Symptom severity	Baseline and twice daily for the first 5 days after enrolment	Acute otitis media faces scale (AOM-FS)	a pictographic scale in which increasing levels of distress are displayed using cartoons of children's faces along with a written description and a numeric scale Range: 1 -	
2	Primary	Symptom severity	Baseline and twice daily for the first 5 days after enrolment	Ear treatment group-5 scores (ETG-5)	Range: 0 - 35 Higher is worse	
3	Secondary	Medication use	Daily	Diary recording	Number of medications used	

Characteristics of included studies	Otitis media				
Study ID	**Taylor 2011**				
4	Secondary	Adverse events	Daily	Diary recording	Parents recorded the presence of any 'other symptoms' that occurred in their child
5	Secondary	Functional status	12-15 days post enrolment	Functional status II revised scale (FSIIR) (14-item)	Includes a set of behavioural items that are consistent with a healthy child and is applicable to all paediatric age
6	Secondary	Visits to healthcare providers	12-15 days post enrolment	Number of visits	Higher is worse
Method of analysis					
Statistics	Mann-Whitney tests were used to assess the statistical significance of differences in ETG-5 scores and AOM-FS. T-tests were used to assess differences in FSIIR scores between children in the two treatment groups				
Population analysed	Intent-to-treat	Modified ITT analysis presumed			
Missing data	Yes	26/120 participants had missing data			

Characteristics of included studies	Otitis media		
Study ID	**Taylor 2014**		
Study reference	Taylor JA, Jacobs J. Homeopathic Ear Drops as an Adjunct in Reducing Antibiotic Usage in Children With Acute Otitis Media. Lobal Pediatric Health. 2014;1:2333794X14559395. Taylor JA, Jacobs J. Homeopathic treatment of respiratory illnesses in children: Results from two randomized trials. Homeopathy: the Journal of the Faculty of Homeopathy. 2016;105(1):15. NCT01003210		
Study design	RCT	Randomisation was performed using a computerised database; randomisation was stratified by study site and in blocks of 4	
Author affiliation	Authors were affiliated with the university of Washington, Seattle, USA		
Source of funds	Study was funded by Standard Homeopathic Company, California, LA		
Declared interests of study authors	2nd author had been a paid consultant for the study sponsor. First author declared no conflicts		
Setting / provider	Outpatient clinics		
Country(s) / region	Washington, USA		
Enrolment period	November 2009 to May 2013		
Length of intervention + follow up	15 day follow up		
Description of population	*N=*	*Description*	
participants	210	Children with acute otitis media	
details	Inclusion criteria: Children 6 mths to 11 years old diagnosed with AOM by a paediatric practitioner who elected to manage the patient with a delayed antibiotic approach. Exclusion criteria: Children who were suspected of having another bacterial illness such as pneumonia or who appeared “toxic” to the clinician, those with myringotomy tubes, perforated tympanic membrane, had received systemic antibiotic treatment within the previous 7 days or homeopathic treatment within the past 30 days.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Otitis media				
Study ID	**Taylor 2014**				
Intervention #1	Non-individualised	105	Participants were prescribed homeopathic ear drops "Hyland's Earache Drops". Administered 3-4 drops up to 3 times daily as needed to relieve symptoms		
Intervention #2	--	--	--		
Comparator #1 (control)	Inactive control	105	Participants received no intervention. Standard care was provided to both groups		
Comparator #2 (other)	--	--	--		
Comparator #3 (other)	--	--	--		
Co-interventions	Standard care consisting of all treatments recommended by the examining clinician, including use of analgesics and directions on when to fill the antibiotic prescription				
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Control (no intervention)
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Antibiotic use	5-7 days and 12-15 days post initial consultation	Number of participants who filled antibiotic prescription	Higher is worse
2	Secondary	Antibiotic use	5-7 days and 12-15 days post initial consultation	Number of participants who either filled the antibiotic prescription or received a new prescription for antibiotics during the study period	Higher is worse
3	Secondary	Symptom severity	Baseline, 5-7 days and 12-15 days post initial consultation	Ear treatment group-5 scores (ETG-5)	Range: 0 - 35 Higher is worse

Characteristics of included studies	Otitis media				
Study ID	**Taylor 2014**				
4	Secondary	Other medication use	Twice daily for 3 days post initial consultation	Diary recording	Number of medications used
5	Secondary	Symptoms	Twice daily for 3 days post initial consultation	Diary recording	Parents recorded the presence of any 'other symptoms' that occurred in their child
6	Secondary	Visits to healthcare providers	5-7 days and 12-15 days post initial consultation	Number of visits	Higher is worse
Method of analysis					
Statistics	ETG-5 scores in children randomized to the homeopathic ear drop or standard therapy alone groups were compared using Mann–Whitney tests. Chi-squared tests were used to assess the statistical significance of differences				
Population analysed	Intent-to-treat	ITT performed			
Missing data	Yes	4/210 participants had missing data for the primary outcome measure. 10/210 participants had missing severity (ETG-5) data at the end of treatment			

Characteristics of included studies	Recurrent URTI (tonsilitis)	
Study ID	**Furuta 2017**	
Study reference	Furuta SE, Weckx LLM, Figueiredo CR. Randomized, double-blind trial on the efficacy of homeopathic treatment in children with recurrent tonsillitis. Rev homeopatia (Sao Paulo). 2017;80(3/4):136-41.	
Study design	quasi RCT	*Randomisation was performed by the homeopathic pharmacist who prepared the medicine (no further details provided). The code was broken only after the end of the treatment of all patients*
Author affiliation	Authors were affiliated with a university in Brazil	
Source of funds	Not reported	
Declared interests of study authors	Not reported	
Setting / provider	Outpatient clinic	
Country(s) / region	Sao Paulo, Brazil	
Enrolment period	March 2000 to September 2001	
Length of intervention + follow up	4 mth intervention and follow up	
Description of population	*N=*	*Description*
participants	40	Children with recurrent tonsillitis

Characteristics of included studies	Recurrent URTI (tonsilitis)		
Study ID	**Furuta 2017**		
details	Inclusion criteria: Children aged 3 to 7 years indicated, indicated tonsillectomy for recurrent tonsillitis while waiting for surgery. Exclusion criteria: Had systemic diseases or immunodeficiency		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	20	Participants had consultations with a homeopath and were prescribed an individualised treatment based on their signs and symptoms, administered in 30cH potency as one single dose. In addition, participants received Baryta carbonica 6cH daily, and isopathic medicine composed of ß-haemolytic Streptococcus, Staphylococcus aureus, Haemophilus influenzae and Tonsil 12cH daily
Intervention #2	--	--	--
Comparator #1 (control)	Placebo	20	Participants also met with the homeopath but received placebo instead of the constitutional remedy (one single dose) and instead of Baryta carbonica 6cH and the isopathic combination (2 daily)
Comparator #2 (other)	--	--	--
Comparator #3 (other)	--	--	--
Co-interventions	Participants who developed acute bacterial tonsillitis were treated with antimicrobial agents		
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Placebo

Characteristics of included studies	Recurrent URTI (tonsilitis)				
Study ID	**Furuta 2017**				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Infection frequency	mthly	Number of acute tonsillitis episodes	Higher is worse
2	Secondary	Otorhinolaryngological assessment	Baseline and last day of treatment	Oral inspection, anterior rhinoscopy and otoscopy	No further details provided
3	--	--	--	--	--
4	--	--	--	--	--
5	--	--	--	--	--
6	--	--	--	--	--
7	--	--	--	--	--
8	--	--	--	--	--
9	--	--	--	--	--
10	--	--	--	--	--

Characteristics of included studies	Recurrent URTI (tonsilitis)				
Study ID	**Furuta 2017**				
11	--	--	--	--	--
12	--	--	--	--	--
Method of analysis					
Statistics	Statistical analysis was performed by means of Fisher's exact test or an extension for tables larger than 2 x 2. The statistical level was set to p= 0.05				
Population analysed	Intent-to-treat	ITT presumed			
Missing data	Yes	7/40 participants had missing data			

Characteristics of included studies	Recurrent URTI (tonsilitis)	
Study ID	**Palm 2017**	
Study reference	Palm J, Kishchuk VV, Ulied A, Fernandez JP, De Jaegere S, Jong MC, et al. Effectiveness of an add-on treatment with the homeopathic medication SilAtro-5-90 in recurrent tonsillitis: An international, pragmatic, randomized, controlled clinical trial. Complementary Therapies in Clinical Practice. 2017;28:181-91 ISRCTN19016626	
Study design	RCT	*Randomisation was performed centrally and in blocks of 2, 4 and 6 using the randomization tool RANSCH. The 3 types of blocks were randomly distributed within each study centre and the investigators did not know the block sizes*
Author affiliation	Authors were affiliated with a number of institutions including universities, hospitals and homeopathic institutions in Germany, Spain, Ukraine, The Netherlands and Sweden	
Source of funds	The study was sponsored by Deutsche Homoopathie-Union, DHU-Arzneimittel GmbH & Co. KG, Karlsruhe, Germany	
Declared interests of study authors	DHU-Arzneimittel GmbH & Co. KG provided funds to many of the authors for their contributions to the study	
Setting / provider	Multi-centre (international) private practices or medical institutions	
Country(s) / region	Germany, Spain and Ukraine	
Enrolment period	25 January 2013 to 15 April 2015	
Length of intervention + follow up	1 year intervention. Maximum 61 wk follow up	
Description of population	*N=*	*Description*
participants	256	Children and adults with recurrent tonsillitis

Characteristics of included studies	Recurrent URTI (tonsilitis)		
Study ID	**Palm 2017**		
details	Inclusion criteria: Female and male patients in the age range 6 - 60 years, diagnosed with moderate recurrent tonsillitis, had at least 3 acute throat infections (ATI) in the past 12 mths of 2 during each of the last two years. Exclusion criteria: ATI at inclusion; peri-tonsillar abscess or acute and chronic respiratory tract disease; obstruction in the pharynx due to enlargement of tonsils; severe comorbidity including previous malignant disease during the past 5 years prior to enrolment; history of intolerance to non-steroidal anti-inflammatory drugs; history or presence of streptococcal complications; previous surgery in the past 6 mths or need for surgery of the nose, paranasal sinuses, adenoids and/or tonsils; presence of neurological and/or psychiatric diseases interfering with patient's assessments; treatment with systemic acting antibiotics, glucose-corticosteroids or immune-modulating medications during 4 wks and with NSAIDs as well as with locally acting antibiotics, glucose-corticosteroids or immune-modulators during the wk prior to inclusion; known or suspected hypersensitivity to the study medication; heavy smoking or known/suspicion of drug or alcohol addiction; women who wanted to become pregnant, were pregnant, breast-feeding or without adequate contraception; prior enrolment into this trial; participation in another clinical trial 3 mths prior to enrolment; incapability of understanding the trial; patients in custody by judicial or official order; staff members or relatives of members related to study		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Non-individualised	132	Participants received homeopathic treatment SilAtro 5-90, taken in 3 treatment periods of 8 wks each during a period of 1 year. Dosage was 1 oral tablet 3 times daily for children <12 years and 2 tablets 3 times per day for everyone else. Participants received 9 study visits and 5 follow up phone calls during the maximum 61 wk study duration
Intervention #2	--	--	--
Comparator #1 (control)	Inactive control	124	Participants received no intervention. Both groups received standard symptomatic treatment for tonsillitis consisting of local antiseptics and local anaesthetics. Antibiotics were given as rescue medication
Comparator #2 (other)	--	--	--
Comparator #3 (other)	--	--	--
Co-interventions	Standard care consisting of local antiseptics and local anaesthetics. Antibiotics were given as rescue medication		
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Control (no intervention)

Characteristics of included studies	Recurrent URTI (tonsilitis)				
Study ID	**Palm 2017**				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Infection frequency	wkly retrospective recording for each day of the previous wk	Diary recording	Mean time between a consecutive ATI within 1 year Higher is better
2	Primary	Infection frequency	wkly retrospective recording for each day of the previous wk	Diary recording	Number of acute throat infections Higher is worse
3	Secondary	Infection duration	wkly retrospective recording for each day of the previous wk	Standardised number of days of recurrent tonsillitis symptoms	Higher is worse
4	Secondary	Symptom severity	wkly retrospective recording for each day of the previous wk	3 point scale measuring severity of 7 recurrent tonsillitis symptoms	Higher is worse
5	Secondary	Symptoms	Day 1 & 11, wk 8, 16, 24, 32, 40, 48 and 60 (end of study)	Number of symptoms present	Higher is worse
6	Secondary	Infection frequency	wk 8 and wk 60 (end of study)	Number of URTIs diagnosed by the investigator	Higher is worse
7	Secondary	Antibiotic use	Day 1 & 11, wk 8, 16, 24, 32, 40, 48 and 60 (end of study)	Number of ATIs that required antibiotic treatment	Higher is worse
8	Secondary	Analgesic use	Day 1 & 11, wk 8, 16, 24, 32, 40, 48 and 60 (end of study)	Proportion of ATIs treated with analgesics	Higher is worse
9	Secondary	Activities of daily living	wkly retrospective recording for each day of the previous wk	Diary recording	The mean standardised number of days where patients' daily activities were affected by recurrent tonsillitis Higher is worse
10	Secondary	Quality of life	Post study visit on Day 1, wk 8, 16, 24, 32, 40, 48 and 60 (end of study)	5 point rating scale. No further details provided	No details provided

Characteristics of included studies	Recurrent URTI (tonsilitis)				
Study ID	**Palm 2017**				
11	Secondary	Treatment outcome	Post study visit on Day 1, wk 8, 16, 24, 32, 40, 48 and 60 (end of study)	Integrative medicine outcome scale	No details provided
12	Secondary	Adverse events	End of study (61 wks)	Number of adverse events	Higher is worse
Method of analysis					
Statistics	Time to event data were analysed within an extension of the Cox proportional hazards approach. A model for recurrent events was calculated using a robust sandwich covariance estimate to fit the data. Treatment-related differences in fractions were calculated by means of Chi-square tests (nominal or 2 categories). Mann Whitney-U test was applied in an exploratory manner to test differences between treatment groups regarding continuously scaled outcome variables				
Population analysed	Intent-to-treat	ITT and per-protocol analysis was performed			
Missing data	Yes	74/256 participants had missing or incomplete data			

Characteristics of included studies	Recurrent URTI		
Study ID	**de Lange de Klerk 1993**		
Study reference	de Lange de Klerk ESM. Effects of homeopathic medicines on children with recurrent upper respiratory tract infections. HomInt R&D Newsletter. 1993. De Lange de Klerk ESM, Blommers J, Kruik DJ, Bezemer PD, Feenstra L. Effect of homoeopathic: Medicines on daily burden of symptoms in children with recurrent upper respiratory tract infections. British Medical Journal. 1994;309(6965):1329-32. De Lange De Klerk ES, Blommers J, Kuik DJ, Feenstra L, Bezemer PD. Effects of individually chosen homeopathic medicines on recurrent URTI in children. A clinical trial - I study methodology. British homoeopathic journal. 1996(85):4-14.		
Study design	RCT	*Participants randomised using permuted blocks (size 4) stratified by age*	
Author affiliation	Authors were affiliated with a University in the Netherlands and a University hospital in Belgium		
Source of funds	The study was funded by a grant from the Dutch Ministry of Welfare, Cultural Affairs and Public Health		
Declared interests of study authors	Not reported		
Setting / provider	Outpatient clinic		
Country(s) / region	Amsterdam, Netherlands		
Enrolment period	March 1987 to January 1992		
Length of intervention + follow up	1 year duration of treatment and follow up		
Description of population	*N=*	*Description*	
participants	170	Children with upper respiratory tract infections	

Characteristics of included studies	Recurrent URTI		
Study ID	**de Lange de Klerk 1993**		
details	Inclusion criteria: Aged between 1 and a half to 10 years of age, had at least 3 upper respiratory tract infections in the past year or had had two such episodes and had otitis media with effusion at the time of the entry examination. Exclusion criteria: Had an adenoidectomy, tonsillectomy or a homeopathic treatment in the past 6 mths, regular medical care or any other chronic condition including chronic non-specific lung disease, untreated dental caries, congenital malformation of the respiratory tract or heart, mental handicap, neurological disorders, height outside the third centile or a history of rheumatic fever, endocarditis, myocarditis or nephritis, did not have at least three symptoms relevant for matching homeopathic medicine, participants whose parents couldn't speak fluent Dutch.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	86	Participants had consultations with a homeopath as often as considered necessary (usually every 2 mths) and we prescribed individualised homeopathic treatment with potencies mainly in the 6th, 30th and 200th decimal
Intervention #2	--	--	--
Comparator #1 (control)	Placebo	84	Participants had consultations with the homeopath as described for the homeopathy treatment group. Participants received a placebo treatment
Comparator #2 (other)	--	--	--
Comparator #3 (other)	--	--	--
Co-interventions	Conventional treatment, as prescribed by the participants' GP		
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Placebo

Characteristics of included studies	Recurrent URTI				
Study ID	**de Lange de Klerk 1993**				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Infection frequency	Daily diary, end of treatment (52 wks)	number of URTI infections	Higher is worse
2	Primary	Symptom severity	Daily diary, end of treatment (52 wks)	Mean daily symptom score	The score has four dimensions: symptoms of the nose, ear, and throat, and general symptoms. The daily score could vary between 0 (no symptoms) to 56 (many
3	Secondary	Symptom free days	Daily diary, end of treatment (52 wks)	Mean % days with symptom score of zero	Higher is better
4	Secondary	Medication use	Daily diary, end of treatment (52 wks)	Total number of antibiotic courses taken (diary recordings)	Higher is worse
5	Secondary	Need for surgery	Daily diary, end of treatment (52 wks)	Number of adenoidectomies & tonsillectomies performed	Range: 13 - 61 Higher is better
6	Secondary	Quality of life	Baseline, 26 wks and end of treatment (52 wks)	Wellbeing questionnaire	Higher is worse
7	--	Adverse events	Daily diary, end of treatment (52 wks)	Number of adverse events	--
8	--	--	--	--	--
9	--	--	--	--	--
10	--	--	--	--	--

Characteristics of included studies	Recurrent URTI				
Study ID	**de Lange de Klerk 1993**				
11	--	--	--	--	--
12					
Method of analysis					
Statistics	T-tests were used to assess differences in means and chi squared tests for differences in proportions. Two tailed p-values and 95% confidence intervals were presented. A stepwise forward multiple linear regression model was used to estimate differences of means of the daily symptom scores adjusted for small differences in prognostic factors at baseline				
Population analysed	Intent-to-treat	Presumed ITT analysis			
Missing data	Yes	61/170 participants had some missing daily symptom outcome data. Of those, 53 participants had missed fewer than 8 days and 4 missed more than a mth over the course of the year			

Characteristics of included studies	Recurrent URTI	
Study ID	**Steinsbekk 2004**	
Study reference	Steinsbekk A, Bentzen N, Fonnebo V, Lewith GT. Randomized controlled trials on treatment by homeopaths and self-treatment with homeopathic medicines: design and protocol. Journal of Alternative & Complementary Medicine. 2004;10(6):1027-32. Steinsbekk A, Bentzen N, Fonnebo V, Lewith G. Self treatment with one of three self selected, ultramolecular homeopathic medicines for the prevention of upper respiratory tract infections in children. A double-blind randomized placebo controlled trial. British Journal of Clinical Pharmacology. 2005;59(4):447-55. Steinsbekk A, Fonnebo V, Lewith G, Bentzen N. Homeopathic care for the prevention of upper respiratory tract infections in children: A pragmatic, randomised, controlled trial comparing individualised homeopathic care and waiting-list controls. Complementary Therapies in Medicine. 2005;13(4):231-8. Steinsbekk A, Lewith G, Fonnebo V, Bentzen N. An exploratory study of the contextual effect of homeopathic care. A randomised controlled trial of homeopathic care vs. self-prescribed homeopathic medicine in the prevention of upper respiratory tract infections in children. Preventive Medicine. 2007;45(4):274-9.	
Study design	RCT	*An independent trial service office provided the randomisation using a computer-based block randomisation with stratification for age groups. The size of the blocks were concealed until the end of the study. Separate randomisation lists were created for arms 3 and 4 of the trial*
Author affiliation	Authors were affiliated with universities in Norway and the UK	
Source of funds	The second author's post is funded by a grant from the Rufford Maurice Laing Foundation	
Declared interests of study authors	Not reported	
Setting / provider	Community	
Country(s) / region	Trondheim, Norway	
Enrolment period	September 2003 to "Summer" 2004	
Length of intervention + follow up	12 wk intervention and follow up	
Description of population	*N=*	*Description*
participants	420	Children with upper respiratory tract infections

Characteristics of included studies	Recurrent URTI		
Study ID	**Steinsbekk 2004**		
details	Inclusion criteria: Children younger than 10 years of age who have been to a medical doctor for URTIs. Exclusion criteria: Concomitant serious disease or daily use of medicines such as antibiotics, steroids (except in inhalators), and cytotoxic agents, and the use of homeopathic medicines in the 3 mths prior to inclusion.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	82	Group B - individualised homeopathic treatment prescribed by a homeopath. Participants received an initial consultation and were prescribed an individualised homeopathic treatment
Intervention #2	Individualised	126	Group C (arm 3) - self-prescribed homeopathic treatment. Participants completed a baseline questionnaire and received homeopathic treatment based on their results. Treatments were 30c potency, taken orally twice daily, 2 days per wk for 12 wks. In addition, 1 pill up to once per hour during an acute URTI episode was given
Comparator #1 (control)	Inactive control	87	Group A (arm 1) - waiting list control. Participants received no intervention. They were advised to complete 12 wks of diary recordings
Comparator #2 (other)	Placebo	125	Group C (arm 4) - placebo. Participants completed a baseline questionnaire and received a placebo treatment consisting of lactose pills. Placebo pills were taken orally twice daily, 2 days per wk for 12 wks. In addition, 1 pill up to once per hour during an acute URTI episode was given
Comparator #3 (other)	--	--	--
Co-interventions	Use of any other treatment of the participant's choice other than homeopathic treatments		
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Placebo and inactive control

Characteristics of included studies	Recurrent URTI				
Study ID	**Steinsbekk 2004**				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Symptom severity	Daily	Total symptom score by diary recording	Nine symptoms could be recorded with a daily possible total score range of 0–11 Higher is worse
2	Secondary	Infection duration	Daily	Median number of days participants experienced URTI, by diary recording	Higher is worse
3	Secondary	Infection duration	Daily	Total numbers of URTI episodes that last for 4 days or more by diary recording	Higher is worse
4	Secondary	Medication use	Daily	Number of participants who used antibiotics	Higher is worse
5	Secondary	Medication use	Daily	Total number of days with painkillers/antipyretic drugs by diary recording	Higher is worse
6	Secondary	Medical consultations	Daily	Total number of consultations with a medical doctor by diary recording	Higher is worse
7	--	--	--	--	--
8	--	--	--	--	--
9	--	--	--	--	--
10	--	--	--	--	--

Characteristics of included studies	Recurrent URTI				
Study ID	**Steinsbekk 2004**				
11	--	--	--	--	--
12					
Method of analysis					
Statistics	Missing data was replaced with the average of the recorded values carried forward. All data was analysed descriptively. Confirmatory testing of the main outcome measure was done based on intention-to-treat principle. All outcome measures were tested using a nonparametric test (Mann-Whitney) because of the expected nonparametric nature of the data. The tests were done separately for arm 1 versus arm 2 and for arm 3 versus 4				
Population analysed	Intent-to-treat	ITT analysis performed			
Missing data	Yes	79/420 participants withdrew from the study			

Characteristics of included studies	Recurrent UTIs		
Study ID	**Pannek 2019**		
Study reference	Pannek J, Pannek-Rademacher S, Jus MS, Wollner J, Krebs J. Usefulness of classical homeopathy for the prophylaxis of recurrent urinary tract infections in individuals with chronic neurogenic lower urinary tract dysfunction. J Spinal Cord Med. 2019;42(4):453-9. NCT01477502		
Study design	RCT	Quasi-randomised	*Participants were randomised into treatment groups (method of randomisation not provided) once all 10 participants in the control group completed the study, recruitment stopped and allocation by randomisation was abandoned*
Author affiliation	Authors were associated with the Swiss Paraplegic Centre and homeopathic clinics in Switzerland		
Source of funds	The dipstick tests used in the study were sponsored by Swiss Medical Solution AG, Switzerland. The study received financial support (urine cultures, homeopathic consultations, costs related to the questionnaires) by a grant from the Dr. B. K. Bose Stiftung für Homöopathie, (formerly the Sokrates foundation, Zug, Switzerland)		
Declared interests of study authors	The authors declared no conflicts of interest		
Setting / provider	Outpatient clinic		
Country(s) / region	Switzerland		
Enrolment period	December 2011 to June 2015		
Length of intervention + follow up	12 month intervention		
Description of population	*N=*	*Description*	
participants	46	Spinal cord injury (SCI) sufferers with recurrent UTIs	
details	Inclusion criteria: Three or more UTIs in the previous year, Exclusion criteria: Time since SCI <12 months, no urodynamically proven neurogenic lower urinary tract disfunction (NLUTD), age < 18 years, lack of comprehension, ongoing homeopathic treatment		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	29	Participants were assessed by a homeopathy and prescribed a homeopathic treatment based on their specific medical history. Treatment was in liquid high potency form, taken orally

Characteristics of included studies	Recurrent UTIs					
Study ID	**Pannek 2019**					
Intervention #2	--	--	--	--	--	--
Comparator #1 (control)	Inactive control	17	control (no intervention)			

Characteristics of included studies	Recurrent UTIs					
Study ID	**Pannek 2019**					
Comparator #2 (other)	--	--	--	--	--	--
Comparator #3 (other)	--	--	--	--	--	--
Co-interventions	Standard prophylaxis consisting of urine acidification with either L-methionine, 3 × 500 mg, or cider vinegar, one teaspoon in 1 glass of water, thrice daily, and cranberry extracts. In patients with recurrent E. coli UTI, oral immunotherapy with a commercially available preparation of lyophilized E. coli was added					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			control (no intervention)	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	
1	Primary	Infection frequency	Every month for 12 months	Number of UTIs	Higher is worse	
2	Secondary	Quality of life	Baseline and end of treatment (12 months)	EQ-5D	Higher is better	
3	Secondary	Quality of life	Baseline and end of treatment (12 months)	Satisfaction with life scale	Higher is better	
4	Secondary	Quality of life	Baseline and end of treatment (12 months)	King's health questionnaire	Higher is worse	
5	Not specified	Homeopathy satisfaction	Baseline and end of treatment (12 months)	Homeopathic questionnaire and visual analogue score (VAS)	Higher is worse for VAS scores. No details provided for homeopathic questionnaire	
Method of analysis						
Statistics	The Wilcoxon signed-rank test and the Wilcoxon rank-sum test were used to investigate the differences between the time points and the groups at the specific time points, respectively. Differences in proportions between the groups were tested using Fisher's exact test. The statistical analyses were performed using the R software environment					
Population analysed	Other (provide details)	Specified ITT - participants without follow up data were not analysed				
Missing data	Yes	11/46 participants withdrew from the study. No adjustments made for missing data				

Characteristics of included studies	Recurrent vulvovaginal candidiasis		
Study ID	**Witt 2009**		
Study reference	Witt A, Kaufmann U, Bitschnau M, Tempfer C, Ozbal A, Haytouglu E, et al. Monthly itraconazole versus classic homeopathy for the treatment of recurrent vulvovaginal candidiasis: a randomised trial. BJOG: An International Journal of Obstetrics & Gynaecology. 2009;116(11):1499-505. NCT00895453		
Study design	RCT	*Participants randomised by computerised randomisation list.. No information provided on allocation concealment*	
Author affiliation	Authors were associated with a university and hospital in Vienna, Austria		
Source of funds	The authors declared there were no sources of funding		
Declared interests of study authors	The authors declared no conflicts of interest		
Setting / provider	Outpatient clinic		
Country(s) / region	Vienna, Austria		
Enrolment period	January 200 to March 2006		
Length of intervention + follow up	Homeopathy group - 12 month intervention (monthly follow-up visits for 6 months, then bi-monthly follow-up visits for another 6 months). Comparator groups - 6 month intervention followed by bi-monthly follow up visits without treatment for 6 months		
Description of population	*N=*	*Description*	
participants	150	Adult women with recurrent vulvovaginal candidiasis	
details	Inclusion criteria: At least 18 years old, at least 4 episodes of Candida vaginitis in previous year and complained of symptoms of acute Candida vaginitis at first presentation at hospital Exclusion criteria: Pregnancy, mixed infections, infection with Candida glabrate or Candida krusei and positive HIV or hepatitis status		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	50	Participants treated with high potencies of a single homeopathic remedy according to their condition, for a treatment duration of 12 months. Participants were followed monthly during the first 6 months and bimonthly for another 6 months

Characteristics of included studies	Recurrent vulvovaginal candidiasis					
Study ID	**Witt 2009**					
Intervention #2	--	--	--	--	--	--
Comparator #1 (control)	Active control	50	Participants received intraconazole as a single-day treatment of 200mg bid twice weekly through 4 weeks, maintenance regimen consisting of itraconazole 200mg bid once a month through 6 months. Followed by bimonthly follow-up visits without treatment for 6 months			

Characteristics of included studies	Recurrent vulvovaginal candidiasis					
Study ID	**Witt 2009**					
Comparator #2 (other)	Active control	50	Participants received single-day treatment of 200mg bid itraconazole twice weekly through 4 weeks. Maintenance regimen consisted of itraconazole 200mg bid one a month through 6 months + one tablet of a vaginal lactobacilli/6 days, monthly. Followed by bi-monthly follow-up visits without treatment for 6 months			
Comparator #3 (other)	--	--	--	--	--	--
Co-interventions	None reported					
Is comparator clearly inactive?	No	Comparison=other			active control	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	
1	Primary	Treatment cure	10 visits over 12 months	Microscopic evaluation and culture	Number of patients free of culture-detectable Candida	
2	Primary	Infection recurrence	10 visits over 12 months	Microscopic evaluation and culture	time from a status of candida-free vaginal culture to recurrence of culture-detected vaginal Candida infection	
3	Primary	Vulvovaginal candidiasis complaints	10 visits over 12 months	VAS	Range: 0-100 Higher is worse	
4	Primary	Satisfaction with treatment	Not specified	Candida infection in the three study groups.	Higher is worse	
5	--	--	--	--	--	
Method of analysis						
Statistics	Chi squared tests were used for comparison of frequencies and cross tabulations and t-test was used on means. A Kaplan–Meier curve was used for evaluating the time to culture-free and time to relapse. A log-rank test was used to compare the three treatment groups. Univariate and multivariate linear regression models with VAS scores as the dependent variable and patient age and education (<5 school years versus >5 school years) as the independent variables were used					
Population analysed	Other (provide details)	Per-protocol analysis based on data of 71 participants who completed all 12 months of the study period				
Missing data	Yes	79/150 participants had missing data (either withdrew from the study or lost to follow up)				

Characteristics of included studies	ANXIETY		
Study ID	**Baker 2003**		
Study reference	Baker DG, Myers SP, Howden I, Brooks L. The effects of homeopathic Argentum nitricum on test anxiety. Complementary Therapies in Medicine. 2003;11(2):65-71		
Study design	RCT	An independent staff member used a random number generator program to generate a randomisation schedule	
Author affiliation	Universities of Queensland and Southern Cross, Lismore Australia		
Source of funds	Funding not specified except for the contribution of Brauer Biotherapies Pty Ltd (Adelaide) in the manufacture of the test preparations		
Declared interests of study authors	Interests not specified by study authors		
Setting / provider	University setting		
Country(s) / region	Australia		
Enrolment period	Study dates not reported		
Length of intervention / follow up	4 consecutive days. Follow up completed within 1 week		
Description of population	*N=*	*Description*	
participants	70	University students experiencing **state test anxiety**	
details	*Inclusion criteria:* Subjects aged between 18 and 60 years inclusive; subjects scored 50 or greater on the Benson RTA; willing to stop all current treatments for the period f the study; willing to comply with the study protocols; willing to receive a placebo on random, double-blind allocation; provides informed consent *Exclusion criteria:* Females who are pregnant or lactating; current psychiatric illness or dementia; history of significant reactions to any food or medications; any significant disease or disorder; needing to take any medications during the period of the study; had any reaction to silver nitrate or its derivatives; low dose sensitivity to alcohol; any condition that, in the opinion of the investigators, might be detrimental to the health of the subject or might interfere with the study objective		

Characteristics of included studies	ANXIETY		
Study ID	**Baker 2003**		
Description of intervention/comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	ANXIETY				
Study ID	**Baker 2003**				
Intervention #1	21	Non-individualised	**Traditionally prepared** oral Argentum nitricum 12x preparation - 5 drops in 30ml of water twice a day for 4 consecutive days. The liquid was to be held in the mouth for 30 seconds before swallowing and taken at least 30 minutes away from any oral intake including smoking and toothpaste. Preparation available commercially in Australia and manufactured by Brauer Biotherapies Pty Ltd (Adelaide)		
Intervention #2	18	Non-individualised	**Radionically-prepared** oral Argentum nitricum 12x preparation - 5 drops in 30ml of water twice a day for 4 consecutive days. The liquid was to be held in the mouth for 30 seconds prior to swallowing and taken at least 30 minutes away from any oral intake including smoking and toothpaste. Supplied by Brauer Biotherapies Pty Ltd (Adelaide) from the same alcohol/water mixture used for the traditionally prepared preparation		
Comparator #1 (control)	23	Placebo	Supplied by Brauer Biotherapies Pty Ltd (Adelaide) from the same alcohol/water mixture used for the traditionally prepared preparation		
Comparator #2 (other)	--	--	--		
Comparator #3 (other)	--	--	--		
Co-interventions	--				
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Anxiety symptoms	Baseline, end of treatment (day 4 + within one week of completion)	Revised Test Anxiety Scale (20-items)	4 dimensions measured on a 4-point Likert scale. Higher score means worse test anxiety
2	Secondary	Anxiety symptoms	Baseline, end of treatment (day 4 + within one week of completion)	Test Anxiety Scale (37-items)	1978 version. Higher score means worse test anxiety

Characteristics of included studies	ANXIETY				
Study ID	**Baker 2003**				
3	Secondary	Equivalence with *A. nitricum* profile	Baseline	A. nitricum profile questionnaire (36-items)	Total score out of 40, using a 5 point Likert scale. Reported as % subjects matching the profile

Characteristics of included studies	ANXIETY	
Study ID	**Baker 2003**	
4	--	
5	--	
6	--	
7	--	
8	--	
Method of analysis		
Statistics	Statistical analysis conducted using the SPSS for Windows 10.0.5. Parallel sets of analyses were run for the TAS and RTA variables. ANCOVA was used with the post-score as the dependent variable, the pre-score as the covariate and the treatments as the factor. Sums of squares were sequentially partitioned so that the post-scores were adjusted for pre-scores. Alpha was set at 0.05.	
Population analysed	Per protocol	Data relevant to those who withdrew (three subjects) was not included in the analysis. Five subjects were lost to follow-up
Missing data	Yes	8/60 (13.33%) missing data. The study authors did not account for missing data

Characteristics of included studies	ANXIETY		
Study ID	**Bonne 2003**		
Study reference	Bonne O, Shemer Y, Gorali Y, Katz M, Shalev AY. A randomized, double-blind, placebo-controlled study of classical homeopathy in generalized anxiety disorder. Journal of Clinical Psychiatry. 2003;64(3):282-7		
Study design	RCT	A senior member of the clinic performed randomisation, which was stratified for sex with simple random assignment within each subgroup	
Author affiliation	Hadassah University Medical School, Jerusalem, Israel and the Israeli Association of Complementary Medicine, Tel Aviv, Israel.		
Source of funds	The authors reported no financial affiliation or other relationship relevant to the subject matter of this article.		
Declared interests of study authors	Interests not specified by study authors		
Setting / provider	Community setting recruited through local newspaper advertisements		
Country(s) / region	Jerusalem, Israel		
Enrolment period	Study dates not reported		
Length of intervention / follow up	Single dose at the beginning of the study repeated 5 weeks later if homeopath deemed necessary. Follow up completed at 10 weeks		
Description of population	*N=*	*Description*	
participants	44	Adults diagnosed with DSM-IV **Generalised Anxiety Disorder**	
details	*Inclusion criteria: >18,* DSM-IV diagnosis of GAD, absence of additional DSM-IV Axis I and II diagnoses, HAM-A score above 20 and HAM-D score below 18. Free of medication for at least 1 month before screening. Psychotherapy was allowed if initiated at least 6 months before beginning the trial. *Exclusion criteria:* Not reported		

Characteristics of included studies	ANXIETY		
Study ID	**Bonne 2003**		
Description of intervention/comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	ANXIETY					
Study ID	**Bonne 2003**					
Intervention #1	22	Individualised	One classical homeopath assessed and prescribed an **individualised single dose** within 4 days of psychiatric examination. A repeat single dose was taken at 5 weeks if deemed necessary by the homeopath. Most participants received a potency of 1M and the rest received a potency of 200CH. **16 different remedies** were given at the start and **5 were changed at week 5**. No more than 2 participants received any single medication			
Intervention #2	--	--	--			
Comparator #1 (control)	22	Inactive control	Administered as per intervention			
Comparator #2 (other)					--	
Comparator #3 (other)					--	
Co-interventions	--					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Anxiety symptoms	Baseline, mid study (week 5), end of treatment (week 10)	Hamilton Rating Scale for Anxiety (HAM-A)	14-item scale with a total score of 0-56.	Higher score means worse anxiety
2	Secondary	Depression	Baseline, mid study (week 5), end of treatment (week 10)	Hamilton Rating Scale for Depression (HAM-D)	17-item scale measured on three or five-point scores	Higher score means worse depression

Characteristics of included studies	ANXIETY					
Study ID	**Bonne 2003**					
3	Secondary	Depression	Baseline, mid study (week 5), end of treatment (week 10)	Beck Depression Inventory (BDI)	21-item self-report rating score 0-63	Higher score means worse depression

Characteristics of included studies	ANXIETY					
Study ID	**Bonne 2003**					
4	Secondary	Psychological distress	Baseline, mid study (week 5), end of treatment (week 10)	Brief Symptom Inventory (BSI)	53-item self-report scale covering 9 symptom dimensions	Higher score means worse distress
5	Secondary	Psychological wellbeing	Baseline, mid study (week 5), end of treatment (week 10)	Psychological General Well-being Index (PGWB)	22-items rated on a 6-point scale assessing 6 domains up to total of 110	Higher score means better psychological well-being
6	Secondary	Anxiety	Baseline, mid study (week 5), end of treatment (week 10)	State Anxiety Inventory (SAI)	20 self-report items on a 4-point Likert scale	Higher score means worse anxiety
7	Secondary	Anxiety	Baseline, mid study (week 5), end of treatment (week 10)	Trait Anxiety Inventory (TAI)	20 self-report items on a 4-point Likert scale. Evaluates a person's anxiety proneness	Higher score means worse anxiety
8	Secondary	Subjective distress	Baseline, mid study (week 5), end of treatment (week 10)	Visual Analogue Scale (VAS)	A 10cm line with two end-points representing 0 (no pain) and 10 (pain as bad as it could possibly be)	Higher score means worse distress
Method of analysis						
Statistics	Group, time and interaction effects for each scale were examined using ANOVA with repeated measures, with medication status as grouping variable and time as a repeated-measure factor. The chi-square statistic was used to examine the distribution of responders in placebo and drug-treated groups. As an additional check MANOVA with repeated measures concurrently for all rating scales was completed, again with medication status (drug/placebo) as grouping variable and time as repeated-measure factor.					
Population analysed	Intent-to-treat	Modified ITT. Only study completers were considered for statistical analysis of results. As a check, a last-observation-carried-forward analysis was performed for all participants for whom data was available for the mid-study assessment				
Missing data	Yes	The study authors did not account for missing data but stated it would be highly unlikely to change the results				

Characteristics of included studies	ANXIETY		
Study ID	**Parewa 2021**		
Study reference	Parewa M, Burman AS, Brahma A, Rutten L, Sadhukhan S, Misra P, et al. Individualized Homeopathic Medicines in the Treatment of Generalized Anxiety Disorder: A Double-Blind, Randomized, Placebo-Controlled, Pilot Trial. Complementary Medicine Research. 2021;28(5):407-17 Clinical trial number: CTRI/2018/03/012685		
Study design	RCT	Other (specify)	Random sequence generated by permuted randomization method by a third party who was not permitted to persuade the study in any way
Author affiliation	National Institute of Homeopathy, Kolkata, India, various universities in West Bengal, India and independent researchers from the Netherlands and India.		
Source of funds	The authors reported not receiving funding for this project.		
Declared interests of study authors	The authors reported no conflict of interest. The trial was carried out as the postgraduate thesis of the corresponding author.		
Setting / provider	Outpatient setting or referral from colleagues		
Country(s) / region	Kolkata, India		
Enrolment period	March 2018 to April 2019		
Length of intervention / follow up	3 months intervention and follow up		
Description of population	*N=*	*Description*	
participants	62	Adults with GAD-2 score of 3 or higher with DSM-V **Generalised Anxiety Disorder**	
details	*Inclusion criteria:* GAD (ICD-10-CM diagnosis code F41.1) diagnosed as per DSM-V criteria with moderate to severe cases of anxiety (GAD-7 scores 10-15 and HAM-A scores 18-30), both male and female patients, aged between 18 and 65 and consent to participate in the study. *Exclusion criteria:* mild (GAD-7 <10 and HAM-A <18) or very severe (GAD-7 >15 and HAM-A >30) anxiety, use of psychoactive medications such as depot neuroleptics within 6 months; any neuroleptic, antidepressant, or anxiolytic within 2 weeks (5 weeks for fluoxetine); daily benzodiazepine therapy within 1 month; and concomitant treatment with any psychotropic drug (except zolpidem for sleep) or any drug with a psychotropic component prior to enrolment into the study, pregnant and puerperal women or lactating mothers, patients with other psychiatric diseases and self reported immune-compromised states, substance abuse and/or dependence, any uncontrolled systemic disease or life-threatening conditions, and patients already availing of homeopathic treatment for any chronic disease		

Characteristics of included studies	ANXIETY		
Study ID	**Parewa 2021**		
Description of intervention/comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	ANXIETY					
Study ID	**Parewa 2021**					
Intervention #1	31	Individualised	A single remedy (verum) prescribed in centesimal potencies by a homeopath (doctor or postgraduate trainee at National Institute of Homeopathy) for 3 months. Each doses consisted of 6-8 globules No.10 moistened with the indicated medicine (preserved in 90% v/v ethanol), to be taken orally on a clean tongue with an empty stomach. Dosage and repition was dependent upon the individual as deemed appropriate by the homeopath. Final selection of the single individualised medicine and dosage was in accordance with the standard homeopathic guidelines and agreement among 3 homeopaths. All the homeopaths involved were affiliated with state councils. The prescriptions on follow-up visits were generated as per relevant homeopathic principles. Homeopathic remedies were permitted to change during the study as and when required in adherence with homeopathic principles.			
Intervention #2	--	--	--			
Comparator #1 (control)	31	Placebo	Placebo was identical to intervention and taken three times a day for the same duration. Patients were also assessed by the 3 homeopaths. Provision was kept to prescribe suitable “acute medicines” (rescue remedies) based on “acute totality” as per homeopathic principles to encounter any adverse or serious adverse events			
Comparator #2 (other)						
Comparator #3 (other)						
Co-interventions	Psychological counselling administered by a conventionally trained medical psychiatrist at monthly intervals for 3 months, received in both the homeopathy and placebo					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Anxiety symptoms	Baseline, end of treatment (3 months)	Generalised Anxiety Disorder 7 (GAD-7) questionnaire (translated Bengali version)	Self-reported 7- item scale. Total score 0-21	Higher score means worse anxiety
2	Secondary	Anxiety symptoms	Baseline, end of treatment (3 months)	Hamilton Anxiety Rating Scale (HAM-A)	14-item scale with a total score of 0-56.	Higher score means worse anxiety

Characteristics of included studies	ANXIETY
Study ID	**Parewa 2021**
3	--

Characteristics of included studies	ANXIETY	
Study ID	**Parewa 2021**	
4	--	
5	--	
6	--	
7	--	
8	--	
Method of analysis		
Statistics	Group differences were tested at baseline and after 3 months by chi-square tests, unpaired t tests and multiple linear regression models. Dependent, continuous observations at baseline and after 3 months were compared using paired t test. Significant level was set at two-tailed alpha of <0.05. No interim and subgroup analyses were performed. Statistical analysis was carried out using Statistical Package for the Social Sciences version 23.0.	
Population analysed	Intent-to-treat	Intention to treat sample was analysed. Three participants from the homeopathy group and 3 participants from the placebo group dropped out from the trial so these missing values were estimated.
Missing data	Yes	Missing values were substituted by regression means.

Characteristics of included studies	ANXIETY		
Study ID	**Fux-Noy 2018**		
Study reference	Homeopathic Combination before Dental Treatment for Anxiety Reduction in Children – Pilot Study A. Noy, O. Bachar Lev, E. Yodko, J. Shapira, S. Faibis, D. Steinberg, et al. 2018		
Study design	quasi RCT	crossover trial	Toss of a coin used to allocate groups.
Author affiliation	Hadassah School of Dental Medicine, Jerusalem, Israel.		
Source of funds	Funding not specified by study authors.		
Declared interests of study authors	Interests not specified by study authors.		
Setting / provider	University setting, parents of eligible children invited		
Country(s) / region	Hadassah, Israel		
Enrolment period	Study dates not reported.		
Length of intervention / follow up	Morning and evening the day before and morning of the dental treatment. Repeated at least one week later for second dental treatment. Follow up completed day of dental treatment		
Description of population	*N=*	*Description*	
participants	22	Healthy children exhibiting some degree of **dental anxiety**	
details	*Inclusion criteria* : healthy 5-9 years-old children, not taking any medications, that needed at least two similar dental treatments and who were cooperative but exhibited some degree of anxiety on the initial diagnostic appointment *Exclusion criteria:* Recent use of other homeopathic remedies or medications		

Characteristics of included studies	ANXIETY		
Study ID	**Fux-Noy 2018**		
Description of intervention/comparator	*n=*	Type of intervention	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*

Characteristics of included studies	ANXIETY					
Study ID	**Fux-Noy 2018**					
Intervention #1	Non-individualised	11	The homeopathic combination comprised of a mixture of Ambra grisea 7cH/Arsenicum album 7cH/Gelsemium sempervirens 9cH/Ignatia amara 9cH/alcohol 18% and was suggested by a specialist in the Integrative and Complementary Medicine Centre, Jerusalem. Ten drops of the combination were taken in the morning and evening on the day before the treatment and on the morning of the treatment day, 2 hours before treatment.			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	11	Administered as per intervention			
Comparator #2 (other)						
Comparator #3 (other)						
Co-interventions	Dental treatment (restorative only), performed 9am to 12pm, was carried out using behaviour management techniques. Patients received inhaled sedation using nitrous oxide					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Anxiety	Before dental treatment and 15 minutes after it ended	Serum salivary cortisol levels	High serum levels of cortisol are found as a reaction to stress	
2	Primary	Anxiety	Before dental treatment and 15 minutes after it ended	Salivary α-amylase levels	Salivary α-amylase levels change as a result of mental and physical stress.	

Characteristics of included studies	ANXIETY				
Study ID	**Fux-Noy 2018**				
3	Not specified	Anxiety	Before dental treatment and 15 minutes after it ended	Facial Image Scale (FIS)	Measures subjective anxiety in children in the dental setting (score 1-5) Higher score means worse anxiety

Characteristics of included studies	ANXIETY				
Study ID	**Fux-Noy 2018**				
4	Not specified	Behaviour	During the dental treatment	Houpt Scale	Measures behaviour in a scale of 1-6 Higher score means better behaviour
5	--				
6	--				
7	--				
8	--				
Method of analysis					
Statistics	To evaluate quantitative variables between two independent groups Wilcoxon test was applied. Spearman's test was used for multivariable correlations. Statistical significance was set at p<0.05.				
Population analysed	Per protocol	11/22 participants analysed. Per protocol analysis assumed.			
Missing data	Yes	The study authors did not account for missing data.			

Characteristics of included studies	ANXIETY	
Study ID	**Dimpfel 2016**	
Study reference	Psychophysiological Effectiveness of Calmvalera Hevert Tablets as Measured by EnkephaloVision in Anxious Subjects during Audio-Visual Cognitive and Emotional Challenges: A Double-Blind, Randomized, Placebo-Controlled, 2-Armed, Phase IV Study in Parallel Design W. Dimpfel, S. Tausend, S. Suliman and G. N. Chiegoua Dipah Journal of Behavioral and Brain Science 2016 Vol. 06 Pages 404-431	
Study design	quasi RCT	Not reported
Author affiliation	University in Germany, Hevert-Arzneimittel, Germany, NeuroCode Ag, Germany	
Source of funds	Funding not specified by study authors.	
Declared interests of study authors	Interests not specified by study authors.	
Setting / provider	Community setting recruited by advertisements in newspapers	
Country(s) / region	Germany	
Enrolment period	Study dates not reported.	
Length of intervention / follow up	Single dose of intervention and follow up completed that day	
Description of population	*N=*	*Description :*
participants	24	Healthy adults with **test anxiety** as determined by PAF-S score
details	*Inclusion criteria:* PAF-S score above 60 aged 18-40 *Exclusion criteria:* Acute or chronic disease with an impact on the study, which becomes obvious by case history or clinical examination (i.e. also Hamilton depression scale), clinically relevant pathological findings from clinical and laboratory findings, clinically relevant allergic symptoms, detection of alcohol at the time of initial examination (screening day SC) or on study day A (positive alcohol test) or by case history, detection of drugs (positive drug test) at the time of initial examination (screening day SC), consumption of clinically relevant medication during last fourteen days before and during the active study period based on the notification of the subject or his case history, consumption of medication with primarily central action (i.e. psychotropic drugs or centrally acting antihypertensives), known intolerance/hypersensitivity (allergy) to plant derived extracts (Cimicifuga, Cocculus, Passiflora, Valeriana etc.) or any of the ingredients of the investigational product (anamnestic), presence of a rare genetic disease such as fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltose deficiency (anamnestic), BMI (Body Mass Index) <18 or >32, consumption of unusual quantities or misuse of coffee (more than 4 cups a day), tea (more than 4 cups a day) or tobacco (more than 20 cigarettes per day), smoking on study day A, participation in another clinical trial within the last 60 days, positive pregnancy test (study day A), lactation, cancellation of informed consent	

Characteristics of included studies	ANXIETY		
Study ID	**Dimpfel 2016**		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*

Characteristics of included studies	ANXIETY					
Study ID	**Dimpfel 2016**					
Intervention #1	Non-individualised	12	Six tablets of Calmvalera hevert tablets (registration no. 77957.00.00) at a time were taken at on the experimental day (Day A) post-randomisation and after the first presentation. Participants then waited in the lounge for 90 minutes before watching a second presentation. The presentation consisted of a gong, then a fixed cross, then a series of emotional and cognitive challenges. One tablet contained a combination of 9 different active ingredients: Cimicifuga Trit. D3 20 m, Cocculus Trit. D4 20 mg, Cypripedium pubescens Trit. D4 10 mg, Ignatia Trit. D6 40 mg, Lilium tigrinum Trit. D6 20 mg, Passiflora incarnata Trit. D3 40 mg, Platinum metallicum Trit. D8 20 mg, Valeriana Trit. D2 20 mg, Zincum valerianicum Trit. D3 20 mg				
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	12	Administered as per intervention			
Comparator #2 (other)						
Comparator #3 (other)						
Co-interventions	--					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Not specified	Brain electric activity	Before therapy and 90 minutes after therapy	Neurocode tracking (dynamic quantitative EEG recording)	Spectral power and spectral frequency changes on EEG and Eye-tracking	
2	Not specified	Cognitive function	Before therapy and 90 minutes after therapy	Memory test	Mental performance measured in cognitive tests	

Characteristics of included studies	ANXIETY				
Study ID	**Dimpfel 2016**				
3	Not specified	Executive function	Before therapy and 90 minutes after therapy	Stroop test	Mental performance tests that measure selective attention capacity, processing speed, and overall executive processing abilities

Characteristics of included studies	ANXIETY	
Study ID	**Dimpfel 2016**	
4		
5		
6		
7		
8		
Method of analysis		
Statistics	For explorative statistical evaluation the nonparametric Wilcoxon test was used. For mathematical differentiation of the different mental loads the linear discriminant analysis according to Fisher was used.	
Population analysed	Other (provide details)	Analysis was not specified and no patients withdrew.
Missing data	Yes	

Characteristics of included studies	DEPRESSION		
Study ID	Adler 2009		
Study reference	Adler UC, Paiva NM, Cesar AT, Adler MS, Molina A, Padula AE, et al. Homeopathic Individualized Q-Potencies versus Fluoxetine for Moderate to Severe Depression: Double-Blind, Randomized Non-Inferiority Trial. Evidence-Based Complementary & Alternative Medicine: eCAM. 2011;2011:520183 Adler UC, Paiva NM, Cesar AT, Adler MS, Molina A, Padula AE, et al. Homeopathic Individualized Q-potencies versus Fluoxetine for Moderate to Severe Depression: Double-blind, Randomized Non-inferiority Trial. Evidence-based complementary and alternative medicine : eCAM. 2009(nep114):[8]-[].		
Study design	RCT	Randomised assignment sequence generated	
Author affiliation	University in Sao Paulo, Brazil		
Source of funds	Source of funding was not reported by study authors.		
Declared interests of study authors	No interests were declared by study authors.		
Setting / provider	Outpatient clinic		
Country(s) / region	Brazil		
Enrolment period	February 2006 to September 2008		
Length of intervention + follow up	8 wks		
Description of population	*N=*	*Description*	
participants	91	Males and females with moderate to **severe depression**	
details	*Inclusion criteria: > 18 years,* met DSM-IV criteria for depression (single or recurrent episode) following a Structured Clinical Interview. Capacity and willingness to give informed consent and to comply with study procedure. *Exclusion criteria:* psychosis, mania, hypomania or any other Axis I disorder except panic disorder, personality disorders, history of seizures, history of alcohol or drug abuse 1 year prior to the screening, antidepressant use up to 30 days before screening, pregnancy or lactation, age < 18 years, MADRS score < 15, recent suicide planning or attempts.		

Characteristics of included studies	DEPRESSION					
Study ID	Adler 2009					
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Individualised	48	One drop of the prescribed Q-potency, three times a wk (on Mondays, Wednesdays and Fridays), in the morning, before breakfast. Changed remedy, potency or posology prescription if no response after 4 wks			
Intervention #2	--	--	--			
Comparator #1 (control)	--	--	--			
Comparator #2 (other)	Active control	43	One 20 mg fluoxetine-hydrochloride capsule once daily, in the morning, after breakfast. Increased to 20mg twice daily if no response after 4 wks.			
Comparator #3 (other)						
Co-interventions	All participants took a placebo for the alternate treatment to maintain blinding.					
Is comparator clearly inactive?	No	Comparison=other				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptoms of depression	Baseline, mid study (wk 4), end of treatment (wk 8)	MADRS	10 items rated on a 7-point Likert scale. Total score 0-60	Higher score means worse depression

Characteristics of included studies	DEPRESSION					
Study ID	Adler 2009					
2	Secondary	Response rate	Baseline, mid study (wk 4), end of treatment (wk 8)	Decrease of ≥ 50% from baseline MADRS score	<50% means not a responder	
3	Secondary	Rate of remission	Baseline, mid study (wk 4), end of treatment (wk 8)	MADRS score ≤ 10	Score >10 means not in remission	
4	Secondary	Tolerability	Throughout the study	Side effect rating scale of the Scandinavian Society of Psycho-pharmacology	% rate of side-effects and % patients reporting side effects that interfere markedly with performance	Higher score means worse tolerability

Characteristics of included studies	DEPRESSION					
Study ID	Adler 2009					
5	--	--	--	--	--	--
6	--	--	--	--	--	--
7	--	--	--	--	--	--
Method of analysis						
Statistics	The demographic characteristics and duration of illness were compared with Student's t-test for independent samples. Fisher's exact test was used for comparison of marital status and analysis of dropouts between the two groups. Analysis of the MADRS scores follow-up was made with repeated ANOVA, with time as within factor and condition as between factor, and Bonferroni's multiple comparisons method. Response and remission rates were analysed with non-parametric analysis for longitudinal data. A prefixed margin of non-inferiority (Δ) of 1.45 was specified. The non-inferiority analysis included all randomised patients, using a "full analysis set".					
Population analysed	Intent-to-treat	Analysis of MADRS mean scores were carried out for all randomised patients				
Missing data	Yes	Missing data was not accounted for in the analysis				

Characteristics of included studies	DEPRESSION
Study ID	Adler 2011
Study reference	2011 protocol: Adler UC, Kruger S, Teut M, Ludtke R, Bartsch I, Schutzler L, et al. Homeopathy for depression--DEP-HOM: study protocol for a randomized, partially double-blind, placebo controlled, four armed study. Trials [Electronic Resource]. 2011;12:43 2013 study: Adler UC, Kruger S, Teut M, Ludtke R, Schutzler L, Martins F, et al. Homeopathy for Depression: A Randomized, Partially Double-Blind, Placebo-Controlled, Four-Armed Study (DEP-HOM). PLoS ONE [Electronic Resource]. 2013;8(9); e74537
Study design	RCT Block randomisation using a 2:1:2:1 ratio
Author affiliation	Two authors affiliated with Universitatsmedizin Berlin, Germany, one also affiliated with Womens Mental Health Centre in Berlin, Germany, one with a foundation in Essen, Germany, one with Institute of General Practice, Munich, Germany and one with a university in Baltimore, USA.
Source of funds	Funded within the grant of the chair for complementary medicine research by the Carstens Foundation.
Declared interests of study authors	The authors declared that no competing interests exist.
Setting / provider	Outpatient clinic
Country(s) / region	Germany
Enrolment period	September 2010 to March 2011 (early termination)
Length of intervention + follow up	6 wks intervention, follow-up at wks 2, 4 and 6
Description of population	*N=* *Description*
participants	44 Males and females with severe major depression *Inclusion criteria:* men and women aged between 18 and 65 years diagnosed with major depression by a psychiatrist and rated afterwards as moderately severe (HAM-D 17 to 24) by a psychologist. Patients must not have been taking antidepressants or anxiolytic drugs (with the exception of Lorazepam as rescue medication, maximum dose 1.5 mg/day) at the time of inclusion. Capability and willingness to give informed consent and to comply with the study procedures.
details	*Exclusion criteria:* schizophrenia or other psychotic disorders, bipolar affective disorder, schizoaffective disorders, alcohol or other substance abuse, eating disorders, a clinically significant DSM-Axis II (Diagnostic and Statistical Manual of Mental Disorders) disorder at the time of inclusion; severe depression which previously motivated a suicide attempt as defined by the Columbia-Suicide Severity Rating Scale (suicidal ideation of type 4 or 5), up to 3 mths before screening; a clinically significant acute or chronic disease that would hinder regular participation in the study; treatment with antipsychotics, antidepressants, sedatives/hypnotics or mood stabilisers four wks prior to the screening; complementary or alternative treatment used simultaneously to the study (for example acupuncture, phytotherapy, etc.); homeopathic treatment 8 wks prior to study entry; psychotherapy; simultaneous participation in another clinical trial (the last participation in a previous clinical trial must be completed at least three mths prior to screening); concomitant pregnancy or breastfeeding; patients who are assumed to have a linguistic, intellectual or any other reason for not understanding the meaning of the clinical trial and for not complying with the necessary study procedures; institutionalised by a court order; application for a pension.

Characteristics of included studies	DEPRESSION					
Study ID	Adler 2011					
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Individualised	16	Q potency and homeopathic case history: case history for 60–90 minutes at baseline, 30 mins at wks 2, 4 and 6 involving a questionnaire and extensive patient-doctor interaction. One sucrose globule of the prescribed Q-potency (Q2) in 10 ml of 20% alcohol-distilled water solvent dispensed within 3 days of first case history. One drop taken 3 times a wk			
Intervention #2	Individualised	14	Q-potency and conventional case history: case histories for 30 minutes at baseline, 10 minutes follow up at wks 2,4 and 6. Same questionnaire used but less patient-doctor interaction. Q-potencies and dosage as before			
Comparator #1 (control)	Placebo	7	Placebo (one sucrose globule in 10 ml of 20% alcohol-distilled water solvent) and homeopathic case history			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)						
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptoms of depression	End of treatment (wk 6)	HAM-D	17-item scale, range of 0-52	Higher score means worse depression

Characteristics of included studies	DEPRESSION					
Study ID	Adler 2011					
2	Secondary	Symptoms of depression	Mid study (wks 2 and 4)	HAM-D	17-item scale, range of 0-53	Higher score means worse depression
3	Secondary	Response rate	Baseline and end of treatment (wk 6)	Decrease of 50% or more from baseline HAM-D score	Higher score means more patients responded	
4	Secondary	Remission	Baseline and end of treatment (wk 6)	HAM-D	HAM-D score ≤ 7)	Higher score means more patients in remission

Characteristics of included studies	DEPRESSION					
Study ID	Adler 2011					
5	Secondary	Symptoms of depression	Mid study (wks 2 and 4) and end of treatment (wk 6)	BDI	21-item self-report rating score 0-63	Higher score means worse depression
6	Secondary	Health-related quality of life	Mid study (wks 2 and 4) and end of treatment (wk 6)	SF-12	Physical and mental health components. Total score 0-100	Higher score means better physical and mental health functioning
7	Secondary	Safety	Throughout the study	Adverse events		
Method of analysis						
Statistics	All data were analysed solely descriptively without any formal hypothesis testing. Generalised linear models with 2 factors were fitted to each continuously scaled outcome measure (HAM-D Score, BDI-Score, SF-12-Score). The time point was modelled as a within-group factor, type of case taking and type of medication (verum, placebo) as between group factors, and the respective baseline value and the patients expectation as linear covariates. Normal distribution was assumed and Generalised Estimation Equations were used to estimate differences between types of case taking and type of medication. For dichotomous outcomes (responder rate, remission rate) similar linear models were fitted, but the underlying distribution was assumed as binomial and the logit was taken as the link-function. This was an exploratory analysis so no p-values were reported.					
Population analysed	Intent-to-treat	All randomised patients included in the safety outcome, analysis not reported for other outcomes				
Missing data	Not specified	Missing data was not specified in the analysis. 7 patients dropped out in total for reasons not specified.				

Characteristics of included studies	DEPRESSION
Study ID	Katz 2005
Study reference	Katz, T., Fisher, P., Katz. A., Davidson, J & Feder, G. 2005. The feasibility of a randomised, placebo-controlled clinical trial of homeopathic treatment of depression in general practice. Homeopathy: the Journal of the Faculty of Homeopathy, 94(3), 145-152
Study design	RCT *Pilot study, computer-generated random number list.*
Author affiliation	A Group Practice in London, Royal London Homeopathic Hospital, Mental Health and Social Care NHS Trust, Department of Psychiatry North Carolina, USA, Queen Mary's School of Medicine and Dentistry
Source of funds	Supported by grants from the Homeopathic Research Committee and the Blackie Foundation Trust.
Declared interests of study authors	No interests were declared by study authors.
Setting / provider	Community referred from group practice
Country(s) / region	England
Enrolment period	Not specified by authors
Length of intervention + follow up	12 wks intervention (and 1 wk placebo run-in)
Description of population	*N=* *Description*
participants	11 Males and females suffering from a moderate major depressive episode
details	Inclusion criteria: adults aged 18-80 of either sex, suffering from a major depressive episode of moderate severity as defined by the DSM-IV, episode lasting at least 4 wks, score of 17 or higher on the Hamilton Depression Scale Exclusion criteria: lifetime or current diagnosis of schizophrenia or schizoaffective disorder or manic depressive psychosis, any current psychotic features, use of antidepressant in the preceding 2 wks, depot neuroleptics in the preceding 6 mths, electroconvulsive therapy in the preceding 3 mths, lack of clear symptom picture for 1 of the homeopathic medicines available, other contraindications to SSRIs, drug interactions with fluoxetine, previous serious adverse reaction to fluoxetine, drug and alcohol abuse (except smoking) in previous 6 mths, pregnancy and lactation, active physical disease for which medication is being adjusted, illiteracy or poor English, inability to follow protocol, *exclusion after 1 wk run-in period if HAMD score improved by ≥25% or moved into normal range, pathology tests outside entry criteria, complained of serious adverse events, failed to comply with treatment

Characteristics of included studies	DEPRESSION					
Study ID	Katz 2005					
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	1	Active homeopathy from a list of 30 commonly prescribed therapies in the form of lactose pillules which were sucked, chosen by a doctor trained in homeopathy using RADAR decision support software and dummy fluoxetine			
Intervention #2	--	--				
Comparator #1 (control)	Placebo	2	Dummy homeopathy and dummy fluoxetine, both identical to the respective verum medication			
Comparator #2 (other)	Active control	3	Active fluoxetine and dummy homeopathy. Fluoxetine 20 mg capsules taken daily, increased to 40 mg by the psychiatrist after 4 wks if no improvement			
Comparator #3 (other)						
Co-interventions						
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptoms of depression	Study run-in (wk -1), start of study (wk 0), mid (wks 2, 4, 8) and end of treatment (wk 12)	HAM-D	17-item scale, range of 0-52	Higher score means worse depression

Characteristics of included studies	DEPRESSION					
Study ID	Katz 2005					
2	Primary	Symptoms of depression	Study run-in (wk -1), start of study (wk 0), mid (wks 2, 4, 8) and end of treatment (wk 12)	CGI	Measures severity and change in severity from initiation of treatment	Higher score means more severe depression and worsening symptoms since treatment started
3	Secondary	Health-related quality of life	End of treatment (wk 6)	SF-12	Physical and mental health components. Total score 0-100	Higher score means better physical and mental health functioning
4	Secondary	Disability	End of treatment (wk 6)	Work and social disability scale	--	--

Characteristics of included studies	DEPRESSION					
Study ID	Katz 2005					
5	Secondary	Sleep quality	Study run-in (wk -1), mid study (wk 4), end of treatment (wk 12)	PSQI	19 item scale, each measured from 0-3, total score 0-21	Higher score means worse sleep quality
6	Secondary	Safety	Throughout the study	Side effects checklist	--	--
7	Secondary	Safety	Throughout the study	Treatment credibility questionnaire	--	--
Method of analysis						
Statistics	Statistical analysis not discussed by study authors (feasibility trial)					
Population analysed	Intent-to-treat	Intention to treat and completers only analyses carried out.				
Missing data	Yes	5 patients withdrew after randomisation. 3 failed to attend two follow-ups, 1 stopped treatment before the 2nd appointment and one did not want fluoxetine. 4 of the 5 withdrew before definitive entry.				

Characteristics of included studies	DEPRESSION	
Study ID	Viksveen 2014	
Study reference	Study protocol: Vikseen, P. & Relton, C. 2014. Depression treated by homeopaths: A study protocol for a pragmatic cohort multiple randomised controlled trial. Homeopathy: the Journal of the Faculty of Homeopathy, 103(2), 147-152; **Full study**: Vikseen P., Relton, C. & Nicholl, J. 2017. Depressed patients treated by homeopaths: a randomised controlled trial using the "cohort multiple randomised controlled trial" (cmRCT) design. Trials [Electronic Resource], 18, 299; **Article**: Viksveen, P. 2016. Homeopathy in self-reported depression: A pragmatic randomised controlled trial. Homeopathy: the Journal of the Faculty of Homeopathy, 105(1), 24.	
Study design	RCT	Pragmatic cohort multiple randomised controlled trial, simple 1:2 randomisation process using a computer software programme
Author affiliation	The University of Stavanger, Norway and the University of Sheffield, the UK	
Source of funds	Mainly funded through anonymous donations and partial funding from a National Institute for Health Research grant to one of the authors, European Council of Homeopaths and various other homeopathic organisations across Europe	
Declared interests of study authors	The authors declared that there were no conflicting/competing interests	
Setting / provider		Community, recruited from the Yorkshire Health Study cohort in 3 integrated health clinics and 1 medical centre
Country(s) / region	England	
Enrolment period	15 September 2013 to 7 February 2014	
Length of intervention + follow up	Up to 9 mths treatment, patients followed up for 12 mths	
Description of population	*N=*	*Description*
participants	566	Males and females previously reported suffering from long-standing depression or feeling moderately or extremely anxious or depressed
details	Inclusion criteria: Adults aged 18-65 responding to a mood and health screening questionnaire with self-reported depression (scoring at least 10 points on the 9-item PHQ including at least 2 points on question 1 or 2. Exclusion criteria: Self-reported Alzheimer's disease, bipolar disorder, organic brain damage, schizophrenia, schizoaffective disorders, other psychotic disorders, or antisocial personality disorder; having received treatment by a homeopath over the past 3 mths; currently being involved in other health research; or being unable to understand study questionnaires and accompanying information due to reduced intellectual capacity, illiteracy or English language skills	

Characteristics of included studies	DEPRESSION					
Study ID	Viksveen 2014					
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Individualised	185	Treatment was offered for up to 9 mths as an adjunct to usual care. Provided by 7 homeopaths who practiced as they usually did with no restrictions on length or frequency of consultations or medicines prescribed. Other treatment could be started at any point during the trial			
Intervention #2	--	--			--	
Comparator #1 (control)	Inactive control	381	No offer of treatment received. Continued treatment as usual			
Comparator #2 (other)	--	--			--	
Comparator #3 (other)						
Co-interventions						
Is comparator clearly inactive?	No	Comparison=other				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptoms of depression	During the study (6 mths)	PHQ-9	9-item scale scored 0-3, total score 0-27	Higher score means worse depression

Characteristics of included studies	DEPRESSION					
Study ID	Viksveen 2014					
2	Secondary	Symptoms of depression	End of the study (12 mths)	PHQ-9	9-item scale scored 0-3, total score 0-28	Higher score means worse depression
3	Secondary	Anxiety	During the study (6 mths) and end of study (12 mths)	GAD-7	Self-reported 7- item scale. Total score 0-21	Higher score means worse anxiety
4	Secondary	Health-related quality of life	During the study (6 mths) and end of study (12 mths)	EQ-5D	Self-reported 5-component scale. Total score 1-100	Higher score means better quality of life

Characteristics of included studies	DEPRESSION					
Study ID	Viksveen 2014					
5	--	--	--	--	--	--
6	--	--	--	--	--	--
7	--	--	--	--	--	--
Method of analysis						
Statistics	A general linear model was used for the primary analysis, comparing the mean depression (PHQ-9) scores at 6 mths post randomisation in the offer group and no offer groups, and controlling for baseline characteristics. At 12 mths post randomisation, analysis of covariance (ANCOVA) was applied comparing mean outcomes in the offer and no offer groups, including outcomes at 6 and 12 mths, and controlling for baseline characteristics. All statistical exploratory tests were two-tailed with alpha set to 0.05. The 95% confidence interval (CI) for the difference in PHQ-9 scores was also calculated for all comparisons. Instrumental analysis, a type of complier average causal effect analyses was also completed					
Population analysed	Intent-to-treat	Intention-to-treat analysis at 6 and 12 mths				
Missing data	Yes	Four approaches for dealing with missing data were used: no imputation for missing data, multiple imputation, regression imputation and last observation carried forward. Multiple imputation was selected as the primary method. Little's missing completely at random (MCAR) test did not suggest any systematic patterns in missing data				

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Fibert 2015**	
Study reference	*Fibert 2015 - links to 2018a (protocol) *Fibert P. Rationale for a pragmatic randomised controlled trial of the effectiveness of treatment by homeopaths for ADHD. Homeopathy 2016 Feb; 105(1):28-29. *Fibert 2018 - links to Fibert 2018b *Fibert P, Relton C, Peasgood T, Daley D. Protocol for the STAR (Sheffield Treatments for ADHD) project: an internal pilot study assessing the feasibility of the Trials within Cohorts (TwiCs) design to test the effectiveness of interventions for children with ADHD. Pilot Feasibility Stud. 2018 Mar 2;4:61. doi: 10.1186/s40814-018-0250-3. *Fibert P, Relton C. Preliminary Feasibility and Clinical Results of a Pilot Study of Treatment by Homeopaths for Children with ADHD using the Trials within Cohorts (TwiCs) Design. Homeopathy. 2018; 107:55-78. 10.1055/s-0038-1632419. *Fibert P, Peasgood T, Relton C. Rethinking ADHD intervention trials: feasibility testing of two treatments and a methodology. Eur J Pediatr. 2019 Jul;178(7):983-993. doi: 10.1007/s00431-019-03374-z. ISRCTN17723526	
Study design	RCT	Randomisation was performed by an independent statistician in blocks of 6 stratified by age, medication status, and ADHD severity. The randomisation list was housed in the locked drawer of another independent statistician who randomly assigned participants to one of the three groups.
Author affiliation	Authors are affiliated with tertiary institutions in the UK	
Source of funds	The study was funded by the Homeopathic Research Institute	
Declared interests of study authors	First author received PhD funding from the Homoeopathic Research Institute, who had no involvement in this study. Other authors declared no potential conflicts of interest	
Setting / provider	Therapist's usual treatment venues	
Country(s) / region	UK	
Enrolment period	September 2015 to 2016	
Length of intervention + follow up	12 mths	
Description of population	*N=*	*Description*
participants	125	Children with ADHD

Characteristics of included studies	Neurodevelopmental, ADHD		
Study ID	**Fibert 2015**		
details	Cohort: *Inclusion criteria:* Cohort inclusion criteria were children aged 5–18 (inclusive) with a carer-reported diagnosis of ADHD and Conners' Global ADHD Index (CGI) T score of at least 55, and any co-morbidities *Exclusion criteria:* Children with terminal or life-threatening conditions, and families where English was not written or spoken Pilot RCT: *Inclusion criteria:* Carer-reported ADHD diagnosis and CGI T score of 65+. *Exclusion criteria:* Currently receiving treatment by a homoeopath or a nutritional therapist.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	42	Participants attended up to 8 consultations with a homeopath over the course of 1 year and were prescribed individualised homeopathic treatments
Intervention #2	--	**--**	**--**
Comparator #1 (control)	Inactive control	41	No intervention
Comparator #2 (other)	Active control	42	Participants attended up to 8 consultations with a nutritional therapist over the course of 1 year and discussed and agreed upon a suitable diet for the participants to adhere to
Comparator #3 (other)	--	--	--
Co-interventions	None reported		
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Inactive control (no intervention)

Characteristics of included studies	Neurodevelopmental, ADHD					
Study ID	**Fibert 2015**					
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	ADHD symptoms	Baseline, 6, and 12 mths	Conners Global Index (CGI)	10 item index	Rated by carers and teachers. Lower is better
2	Primary	Behaviour	Baseline, 6, and 12 mths	Conners Global Index (CGI)	sub-score: restlessness/ impulsivity (7 items)	Rated by carers and teachers. Lower is better
3	Primary	Emotional function	Baseline, 6, and 12 mths	Conners Global Index (CGI)	sub-score: emotional lability (3 items)	Rated by carers and teachers. Lower is better
4	Secondary	Child health-related quality of life	Baseline, 6, and 12 mths	Child health utility 9 dimensions (CHU-9D)		Rated by carers and teachers. Lower is better
5	--	--	--	--	--	--
6	--	--	--	--	--	--
Method of analysis						
Statistics	Two-tailed tests with significance level (alpha) set to 5%. Each treatment was compared with usual care. Change scores were calculated by subtracting 6-mth scores from baseline scores (lower scores indicate better outcomes). Preference weights were added to health-related quality of life measure CHU 9D. Statistical testing was exploratory since the pilot study was not powered to detect statistical differences. Regression analysis explored the predictive power of the offer of treatment, with analyses controlling for the effects of gender, ADHD severity, and age. Standardised mean differences (SMDs) (Cohen's d) explored the magnitude of the clinical effect and provided estimates for the sample size required in the full trial.					

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Fibert 2015**	
Population analysed	Intent-to-treat	The primary outcome used intention to treat (ITT) analysis. Secondary analyses explored the effect of having a treatment on the outcome (per protocol analysis).
Missing data	Yes	Last observation carried forward was used to impute the missing data in the few instances of missing data in paper Carer questionnaires. Of those randomised, the majority of returned 6-mth (20/29 Hom; 24/28 NT) and 12-mth (16/22 Hom; 16/19 NT) questionnaires were from those who had that treatment. There were 5 instances of missing data in the few paper Carer Questionnaires. Teacher outcomes were potentially available from a maximum of 100 teachers, as 20 carers refused permission for their child's school to be contacted and 4 children were home schooled. 72 baseline, 34 6-mth, and 58 12-mth Teacher Questionnaires were returned. Schools did not return questionnaires consistently: 31 paired baseline and 6-mth questionnaires, 14 paired 6 and 12-mth questionnaires, and 21 paired baseline and 12-mth questionnaires were returned. Thirty-five percent of paired questionnaires were returned by different teachers.

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Frei 2005**	
Study reference	*Frei H, Everts R, von Ammon K, Kaufmann F, Walther D, Hsu-Schmitz SF, Collenberg M, Fuhrer K, Hassink R, Steinlin M, Thurneysen A. Homeopathic treatment of children with attention deficit hyperactivity disorder: a randomised, double blind, placebo controlled crossover trial. Eur J Pediatr. 2005 Dec;164(12):758-67. doi: 10.1007/s00431-005-1735-7. Epub 2005 Jul 27. PMID: 16047154. *Frei 2006a (non-English) Frei H, von Ammon K, Thurneysen A. Treatment of hyperactive children: Increased efficiency through modifications of homeopathic diagnostic procedure. Homeopathy. 2006; 95(3):163-170. doi:10.1016/j.homp.2006.05.007. *Frei H, Everts R, von Ammon K, Kaufmann F, Walther D, Hsu-Schmitz SF, Collenberg M, Steinlin M, Lim C, Thurneysen A. Randomised controlled trials of homeopathy in hyperactive children: treatment procedure leads to an unconventional study design: Experience with open-label homeopathic treatment preceding the Swiss ADHD placebo controlled, randomised, double-blind, cross-over trial. Homeopathy. 2007;96(1):35-41. doi:10.1016/j.homp.2006.11.004. *von Ammon K, Frei H, Kaufmann F, Hsu Schmitz S-F, Steinlin M, Thurneysen A. Homoeopathic RCT embedded in an observational study of children with attention deficit hyperactivity disorder — a successful model of whole-systems CAM research. Focus on Alternative & Complementary Therapies 2007; 12:5-5. *von Ammon K, Sauter U, Frei H, Kretschmar S, Thurneysen A, Frei-Erb Martin. Classical homeopathy helps hyperactive children–a 10-year follow-up of homeopathic and integrated medical treatment in children suffering from attention deficit disorder with and without hyperactivity. Eur J Integr Med. 2012; 4 (S1):73-74. doi:10.1016/j.eujim.2012.07.645.	
Study design	RCT	Randomised, placebo-controlled, crossover trial, embedded in an observational study, involving a run-in phase followed by randomisation of responders and subsequent double-blind crossover period
Author affiliation	Authors were affiliated with the Swiss Association of Homeopathic Physicians or tertiary institutions in Switzerland	
Source of funds	Swiss foundations and institutions: Gertrude von Meissner Foundation, Basel; Software AG Foundation, Darmstadt; Hans Eggenberger Foundation, Zu¨ rich; SNE Foundation, Solothurn; Foundation Homeopathy Pierre Schmidt Gene`ve; PanMedion Foundation, Zu¨ rich; Spagyros AG, Gu¨ mligen; Gudjons Laboratory, Stadtbergen; Swiss Federal Railways (SBB), Berne.	
Declared interests of study authors	Authors declared no conflicts	
Setting / provider	Single centre - Division of Paediatric Neurology of the University Children's Hospital Berne	
Country(s) / region	Switzerland	
Enrolment period	January 2002 to September 2004	
Length of intervention + follow up	14 wks follow-up after crossover trial	
Description of population	*N=*	*Description*
participants	62	Children with ADHD

Characteristics of included studies	Neurodevelopmental, ADHD		
Study ID	**Frei 2005**		
details	Screening phase *Inclusion criteria:* : age between 6 and 16 years, both genders, confirmed ADHD according to DSM-IV criteria and known neuropsychological correlates (greater difficulty in learning, memory, non-automated language tasks, and traditional frontal executive measures), necessity for treatment, absence of any chronic physical, neurological or psychiatric disorders. *Exclusion criteria:* not conforming to rigorous ADHD criteria in the questionnaires Crossover trial *Inclusion criteria:* Patients must reach an amelioration of 50% of the initial CGI value or at least 9 points during the screening phase.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	62	Screening phase: Treatment commenced within 1 mth of confirmation of diagnosis. Individually prescribed homeopathic treatment daily according to the guidelines described by Hahnemann and Boenninghausen; administered as Q (LM) potencies. Medication was adjusted until an optimal treatment was identified for each child; the child then received this medication for the duration of the study. Double-blind phase: 2 parallel groups received verum (V) for 6 wks followed by placebo (P) for 6 wks (arm A: VP), or placebo for 6 wks followed by verum for 6 wks (arm B: PV). Both arms received another 6 wks of open label treatment (arm A: VPV, arm B: PVV) and an additional long-term follow-up under treatment.
Intervention #2	--	**--**	**--**
Comparator #1 (control)	Placebo	62	Participants also had a consultation with a homeopath and received identical placebo containing 20% alcohol
Comparator #2 (other)	**--**	**--**	--
Comparator #3 (other)	**--**	**--**	--
Co-interventions	None reported		
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Placebo

Characteristics of included studies	Neurodevelopmental, ADHD					
Study ID	**Frei 2005**					
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	ADHD symptoms	Baseline (after screening); 6 and 14 wks after crossover; and final assessment (relative timing unspecified)	Conner's global index (CGI)	10-item rating scale containing the most important ADHD symptoms. 0= never, 1= occasionally, 2= often, 3= very often)	Rated by parents
2	Secondary	Behaviour	Baseline (after screening phase) & 6 wks after crossover trial	Questionnaire of Change of Behaviour (QCB)		
3	Secondary	Symptom severity	Baseline (after screening phase) & 6 wks after crossover trial	VLMT and subtests of WISC-III, K-ABC, Verbal Learning Test (VLMT)		
4	Secondary	Symptom severity	Baseline (after screening phase) & 6 wks after crossover trial	Test battery for attention performance (TAP)		
5	--	--	--	--	--	--
6	--	--	--	--	--	--
Method of analysis						
Statistics	Correlated outcome variables analysed with linear mixed model using SAS v8. For selected variables of behaviour and cognitive performance, the within-patient differences between diagnosis and the beginning of the crossover trial were analysed using the Wilcoxon signed rank test. The changes in CGI from diagnosis to later time points were analysed by paired t-test.All significance tests were two-sided. All analyses of secondary endpoints were of an exploratory nature without adjustment for multiple testing.					

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Frei 2005**	
Population analysed	Intent-to-treat	Following the intention-to-treat principle, all 62 patients were included in the analysis.
Missing data	Yes	4/62 withdrawn (1 increasing tics, 2 behavioural disorders, 1 reactive depression)

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Jacobs 2005**	
Study reference	Jacobs J, Williams AL, Girard C, Njike VY, Katz D. Homeopathy for attention-deficit/hyperactivity disorder: a pilot randomized-controlled trial. J Altern Complement Med. 2005 Oct;11(5):799-806. doi: 10.1089/acm.2005.11.799. PMID: 16296913.	
Study design	RCT	A homeopathic pharmacist randomized the subjects in blocks of four using a computerised random number generator, stratified by gender and use or nonuser of stimulant medication. Once assigned to a treatment group, all subsequent prescriptions for that subject were filled according to the initial randomisation.
Author affiliation	Authors were affiliated with tertiary institutions, a research centre or a cancer treatment centre in the US	
Source of funds	The study was funded by a grant from the Centers for Disease Control and Prevention	
Declared interests of study authors	Not reported	
Setting / provider	Community	
Country(s) / region	Seattle, Washington, USA	
Enrolment period	Not reported	
Length of intervention + follow up	Not reported	
Description of population	*N=*	*Description*
participants	43	Children with ADHD

Characteristics of included studies	Neurodevelopmental, ADHD		
Study ID	**Jacobs 2005**		
details	Mean age 9.5 years, 72.7% male (homeopathy group) and 9 years, 81% male (placebo group). 9 were currently taking stimulant medications (5 in the homeopathy group and 4 who received placebo). A comparison of demographic characteristics and baseline values found no significant differences between the two groups. Baseline T-scores for both inattention and impulsivity on the CPT were within the average range for both groups, while the values of the parent and teacher assessments were in the moderate to markedly atypical range. Inclusion criteria: Children 6-12 years of age meeting DSM-IV Criteria for ADHD. Children who were taking stimulant medication were included in the study if their dosage had been stable for 6 mths prior to enrolment and they were still exhibiting symptoms of ADHD Exclusion criteria: Comorbid medical or psychological conditions that influenced behaviour or the ability to complete the study protocol or required the use of medications thought to interfere with homeopathic treatment, such as corticosteroids; home-schooled.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	22	Participants received consultations with a homeopath and were prescribed an individualised homeopathic remedy that best matched their symptoms. Participants received follow up consultations at 6, 12 and 18 wks
Intervention #2	--		
Comparator #1 (control)	Placebo	21	Participants received consultations with a homeopath as described for the homeopathic treatment group, however received placebo medication
Comparator #2 (other)	--		
Comparator #3 (other)	--		
Co-interventions	None reported		
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Placebo

Characteristics of included studies	Neurodevelopmental, ADHD					
Study ID	**Jacobs 2005**					
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	ADHD symptoms	Baseline and wkly during the 18 wks of study	Conners Global Index—Parent (CGI-P)	Higher is worse	Completed by parents
2	Secondary	ADHD symptoms	Baseline, 6, 12 and 18 wks	Connors Parent Rating Scale-Brief (CPRS-B)	Higher is worse	Completed by parents
3	Secondary	ADHD symptoms	Baseline, 6, 12 and 18 wks	Connors Global Index-Teacher (CGI-T)	Higher is worse	Completed by teachers
4	Secondary	Symptom severity	Baseline, 6, 12 and 18 wks	Stimulant Side-Effects Checklist		Part of the ADHD-Symptom Checklist 4 (ADHD-SC4)
5	Secondary	Medication effects; treatment response	Baseline, 6, 12 and 18 wks	Continuous Performance Test (CPT)	Higher is worse	Performed by child. Omission errors, to evaluate attention, and commission errors, which measure impulsivity
6	Secondary	Symptom improvement	Baseline, 6, 12 and 18 wks	Clinical Global Impression–improvement scale (CGI-IS)	Range: 1-7 Higher is worse	Completed by homeopath
Method of analysis						
Statistics	Changes in outcome measures scores before and after intervention measured using ANOVA and categorical data were analysed using chi-square statistics. Repeated measures of ANOVA with one-between subject effect (treatment) and one within-subject effect (time) was performed to determine if there were statistically significant differences in outcome measures. Combined effects of independent variables and intervention on outcome measures before and after the intervention were assessed with multivariable models using ANCOVA.					

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Jacobs 2005**	
Population analysed	Intent-to-treat	All analyses were by intention-to-treat
Missing data	Yes	6/43 participants had missing data

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Lamont 1997**	
Study reference	Lamont J. Homoeopathic treatment of attention deficit hyperactivity disorder: A controlled study. Br Hom J 1997; 86(4):196-200. doi: 10.1016/S0007-0785(97)80044-0. Lamont J. Homeopathic treatment of attention deficit hyperactivity disorder: a controlled study. Biomedical Therapy 1998;16(3):219-222.	
Study design	quasi RCT	Assigned alternately to placebo or homeopathic treatment in the order in which they were referred for testing. Partial crossover, in which the placebo group was given homeopathic medicines and compared against itself
Author affiliation	Not reported	
Source of funds	Not reported	
Declared interests of study authors	Not reported	
Setting / provider	Community	
Country(s) / region	California, USA	
Enrolment period	Not reported	
Length of intervention + follow up	Treatment was given for up to 5 days or until a notable change occurred, with a follow-up interview 10 days after each administration and again about 2 mths after the last medication. Patients could be tried on up to 3 medicines with a 10-day follow-up after each one	
Description of population	*N=*	*Description*
participants	43	Children with ADHD

Characteristics of included studies	Neurodevelopmental, ADHD			
Study ID	**Lamont 1997**			
details	All the children were living in foster homes or with their parents under the supervision of social workers. 35% of the children were Black, 18% Caucasian and 47% Hispanic; 58% were male and 42% female. The average age was 10 years. 6 children were on Ritalin, Cylert or clonidine (anti-ADHD medication). All 6 showed signs of ADHD despite this medication. Inclusion criteria: Children meeting the diagnostic criteria for ADHD; The level of severity of the hyperactive behaviour had to be at or beyond the criteria used in the DSM-IV Exclusion criteria: On anti-ADHD medications for less than 6 wks			
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*	
Intervention #1	Individualised	20	Participants met with a homeopath and were prescribed 6 pills daily at one time, for up to 5 days or until a notable change occurred. The potency of all remedies was 200c. No further medicines were administered after 3 tries, or once the carer reported improvement at the 'much better' level.	
Intervention #2	--	**--**	--	
Comparator #1 (control)	Placebo	23	Participants also met with a homeopath and received an identical placebo. Dosing regimen was as described for the homeopathic treatment group	
Comparator #2 (other)	--	**--**	--	
Comparator #3 (other)	--	**--**	--	
Co-interventions	None reported			
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis		Placebo

Characteristics of included studies	Neurodevelopmental, ADHD					
Study ID	**Lamont 1997**					
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	ADHD symptoms	Rated over the 10-days following administration	5-point scale of observed changes in hyperactivity	much worse (- 2); a little worse (- 1); no change (0); a little better (+ 1); and much better (+ 2)	Rated by parents/carers. Changes in hyperactivity had to be observed in the home and/or reported by teachers at school.
2	--	--	--	--	--	--
3	--	--	--	--	--	--
4	--	--	--	--	--	--
5	--	--	--	--	--	--
6	--	--	--	--	--	--
Method of analysis						
Statistics	Comparison of improvement scores were done using Student's t-test, based on the assumption that samples were drawn from populations of means with equal variances. A two-tailed test of significance was used.					

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Lamont 1997**	
Population analysed	Other (provide details)	Not specified
Missing data	Yes	3 participants from the homeopathy treatment group were excluded from the study. Not specified whether the data was included in analysis

Characteristics of included studies	Neurodevelopmental, ADHD		
Study ID	**Oberai 2013**		
Study reference	Oberai P, Gopinadhan S, Varanasi R, Mishra A, Singh V, Nayak C. Homoeopathic management of attention defi cit hyperactivity disorder: A randomised placebo controlled pilot trial. Indian J Res Homoeopathy 2013;7(4):158-67. CTRI/2011/12/002305		
Study design	RCT	Computer generated random numbers, block size 2. Allocation concealment not reported.	
Author affiliation	1 author affiliated with Central Research Institute, Kottayam, Kerala, India; none specified for remaining authors		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Central Research Institute (Homoeopathy), Kottayam, Kerala, India from June 2009 to November 2011		
Country(s) / region	India		
Enrolment period	June 2009-November 2011		
Length of intervention + follow up	1 year intervention		
Description of population	*N=*	*Description*	
participants	61	Children with ADHD	

Characteristics of included studies	Neurodevelopmental, ADHD			
Study ID	**Oberai 2013**			
details	54 patients analysed under mITT. As per ADHD Index, 13 children were markedly atypical with significant problem H:5; P:8; 24 were moderately atypical with significant problem H:12; P:12 and 17 were mildly atypical with possible significant problem (H: 10; P: 07). Baseline characteristics comparable between groups (p≥0.05). Inclusion criteria: Children in the age group of 6-15 years and meeting the Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) criteria for ADHD; not on any other non-pharmacological intervention like operational therapy, play therapy and behavioural modification Exclusion criteria: Children with any chronic physical or neurological disorder, history of drug abuse, seizure, Tic disorder, Tourette syndrome, severely ill patient requiring hospitalisation and patients who were on anti-ADHD or psychoactive medications in the previous two wks			
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*	
Intervention #1	Individualised	30	Participants received consultations with a homeopath and were prescribed individualised homoeopathic medicine for one year, starting with 0/1 potency, followed by next higher potency, serially, as per need of the case. Instructions to pharmacist: 1 globule (poppy-seed size) of the desired potency dissolved in 120 ml of distilled water, containing 2.4 ml (2% v/v) of dispensing alcohol, pre-mixed in it, followed by 10 uniformly forceful downward strokes against the bottom of the phial. The medicine was given once daily in the morning on an empty stomach as long as improvement continued. Instructions to parents/guardians: Give 10 uniformly forceful downward strokes to the bottle with the hand on a hard surface and take 3 tea-spoonfuls (15 ml) of this solution and mix it in 8 tea-spoonfuls (40 ml) of water in a clean glass after stirring the solution before each dose. One tea spoonful (5 ml) of this solution constituted one dose.	
Intervention #2	--	--	--	
Comparator #1 (control)	Placebo	31	Participants received consultations with a homeopath and received placebo which was similar in all manner to that of the homeopathic group including the process of administration, however constituted un-medicated poppy size	
Comparator #2 (other)	--	--	--	
Comparator #3 (other)	--	--	--	
Co-interventions	Patients with acute complaints were given individualised homoeopathic medicines			
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis		Placebo

Characteristics of included studies	Neurodevelopmental, ADHD					
Study ID	**Oberai 2013**					
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	ADHD symptoms	Baseline and mthly for 12 mths	Conner's Parents Rating Scale-revised: Short (CPRS-R(s))	Higher is worse	4 domains measured (oppositional, cognition problems, hyperactivity, ADHD index
2	Primary	Symptom severity	Baseline and mthly for 12 mths	Clinical Global impression severity scale (CGI-SS)	7 point scale: 1=normal, not at all ill, 7=most extremely ill	Assessed by the investigator and consultant psychiatrist
3	Primary	Symptom improvement	Baseline and mthly for 12 mths	Clinical Global Impression–improvement scale (CGI-IS)	7 point scale: 1=patient very much improved, 7=very much worse	Assessed by the investigator and consultant psychiatrist
4	Secondary	Academic performance	Before and after treatment	Record of academic performance in school		
5	--	--	--	--	--	--
6	--	--	--	--	--	--
Method of analysis						
Statistics	Independent t-test for continuous variable and Chi-square test for categorical variables to assess randomisation effect; ANCOVA; questionnaires compared using a General Linear Model Analysis of covariance (GLM-ANCOVA) for repeated measures; multivariate repeated measures ANOVA for further comparison of all outcome measures; paired t-test for assessing the difference (T12-T0) in individual variable in each group.					

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Oberai 2013**	
Population analysed	Intent-to-treat	Analysed as per modified ITT. 7 children were excluded from analysis after enrolment for not following randomisation.
Missing data	Yes	Missing data were replaced by last assessed value as per the last observation carry forward method (LOCF). Dropouts: 5 from homeopathy and 7 from placebo group (reasons not reported).

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Strauss 2000**	
Study reference	Strauss LC. The efficacy of a homeopathic preparation in the management of attention deficit hyperactivity disorder. Biomed Ther. 2000; 18(2):197-201.	
Study design	quasi RCT	Each group of ten children (Ritalin and non-Ritalin) was randomly divided into two groups of five, a control and an experimental group. Method of randomisation not reported.
Author affiliation	Not reported	
Source of funds	Not reported	
Declared interests of study authors	Not reported	
Setting / provider	Not reported	
Country(s) / region	Republic of South Africa	
Enrolment period	Not reported	
Length of intervention + follow up	60 day treatment period	
Description of population	*N=*	*Description*
participants	20	Children with ADHD

Characteristics of included studies	Neurodevelopmental, ADHD		
Study ID	**Strauss 2000**		
details	10 children currently taking methylphenidate HCl (Ritalin group) and 10 children not taking any medication for their ADHD (non-Ritalin group) . 18 boys and 2 girls. *Inclusion criteria:* not reported *Exclusion criteria:* not reported		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Non-individualised	5	Selenium-Homaccord (selenium and potassium phosphate) administered over 60 days (Ritalin group, experimental)
Intervention #2	Non-individualised	5	Selenium-Homaccord (selenium and potassium phosphate) administered over 60 days (non-Ritalin group, experimental)
Comparator #1 (control)	Inactive control	5	Not described, treatment period 60 days (Ritalin group, control)
Comparator #2 (other)	Inactive control	5	Not described, treatment period 60 days (non-Ritalin group, control)
Comparator #3 (other)	--		
Co-interventions	None reported		
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Inactive control (no intervention)

Characteristics of included studies	Neurodevelopmental, ADHD				
Study ID	**Strauss 2000**				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	ADHD symptoms	Baseline, day 30 and end of treatment (day 60)	Conner's Parents Symptom Questionnaire (PSQ)	No further details provided
2	Primary	Symptom severity	Baseline, day 30 and end of treatment (day 60)	Children's Checking Task (CCT)	No further details provided
3	--	--	--	--	--
4	--	--	--	--	--
5	--	--	--	--	--
6	--	--	--	--	--
Method of analysis					
Statistics	Repeated measures ANOVA and unpaired t-test				

Characteristics of included studies	Neurodevelopmental, ADHD	
Study ID	**Strauss 2000**	
Population analysed	Other (provide details)	Presumed ITT
Missing data	Not specified	

Characteristics of included studies	Neurodevelopmental, learning	
Study ID	**Dhawale 2014**	
Study reference	Dhawale K, Tamboli M, Katawala M, Tambitkar N, Tamboli P. Use of homoeopathic remedies in the management of learning disabilities. Indian J Res Homoeopathy 2014;8(2):87-94. doi: 10.4103/0974-7168.135641	
Study design	quasi RCT	Study was described as randomised, however no details on the randomisation process were provided. Participants were divided into two groups as per their enrolment
Author affiliation	Not reported	
Source of funds	The study was funded by the department of AYUSH, Ministry of Health and Family Welfare, India	
Declared interests of study authors	Authors declared no conflicts	
Setting / provider	Study conducted in 3 schools in Mumbai	
Country(s) / region	Mumbai, India	
Enrolment period	Not reported	
Length of intervention + follow up	12 mth intervention and follow up	
Description of population	*N=*	*Description*
participants	67	Children with dyslexia and dysgraphia

Characteristics of included studies	Neurodevelopmental, learning			
Study ID	**Dhawale 2014**			
details	Inclusion criteria: Aged 8 - 12 years with at least one type of learning disorder diagnosed according to criteria stated in ICD-10. Exclusion criteria: Children with neurological problem, emotional disturbance like depression, mental retardation or lack of educational inputs as causes of learning difficulties.			
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*	
Intervention #1	Individualised	32	Participants had received consultations with a homeopath and were prescribed individualised homeopathic treatments in the 200th potency as single wkly repetitions	
Intervention #2	--	--	--	
Comparator #1 (control)	Placebo	35	Participants received treatment with a placebo, no further details on duration or dosage provided	
Comparator #2 (other)	--	--	--	
Comparator #3 (other)	--	--	--	
Co-interventions	Remedial education			
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis		Placebo

Characteristics of included studies	Neurodevelopmental, learning				
Study ID	**Dhawale 2014**				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Prevalence and changes in reading	3, 6, 9, 12 mths	Results presented as categorical variables	(absent, better, no change and increased) No further detailed provided
2	Primary	Prevalence and changes in writing	3, 6, 9, 12 mths	Results presented as categorical variables	(absent, better, no change and increased) No further detailed provided
3	Primary	Prevalence and changes in written expression	3, 6, 9, 12 mths	Results presented as categorical variables	(absent, better, no change and increased) No further detailed provided
4	Primary	Prevalence and changes in listening comprehension	3, 6, 9, 12 mths	Results presented as categorical variables	(absent, better, no change and increased) No further detailed provided
5	Primary	Prevalence and changes in reading comprehension	3, 6, 9, 12 mths	Results presented as categorical variables	(absent, better, no change and increased) No further detailed provided
6	Primary	Prevalence and changes in associated complaints in the population	3, 6, 9, 12 mths	Results presented as categorical variables	(absent, better, no change and increased) No further detailed provided
Method of analysis					
Statistics	t-tests were used for statistical analyses				

Characteristics of included studies	Neurodevelopmental, learning	
Study ID	**Dhawale 2014**	
Population analysed	Other (provide details)	Details not provided, unable to be determined from the results presented
Missing data	Not specified	Not reported

Characteristics of included studies	INSOMNIA		
Study ID	**Harrison 2013**		
Study reference	Harrison CC, Solomon EM, Pellow J. The effect of a homeopathic complex on psychophysiological onset insomnia in males: a randomized pilot study. Alternative Therapies in Health & Medicine. 2013;19(5):38-43.		
Study design	quasi RCT	One participant from each matched pair selected a remedy from one of two boxes.	
Author affiliation	Two authors from a university in South Africa, one from an NHS treatment centre in the UK		
Source of funds	Financed and supported by the University of Johannesburg		
Declared interests of study authors	No information		
Setting / provider	Community, advertised on university campus and internet		
Country(s) / region	South Africa		
Enrolment period	February 2006 to September 2008		
Length of intervention + follow up	4 wk intervention, no follow up reported		
Description of population	*N=*	*Description*	
participants	34	Men with **chronic primary insomnia**	
details	Inclusion criteria: men aged 18-40, chronic primary insomnia at least 3 days per wk for at least 1 mth Exclusion criteria: females, using any medication or recreational drugs, ingesting more than 20 units of alcohol per wk, mental or psychiatric disorders, sleep disorders such as restless leg syndrome, narcolepsy or obstructive sleep apnoea, medical disorders in which discomfort or pain resulted in the development of insomnia or where sleeplessness was concomitant to their illness		

Characteristics of included studies	INSOMNIA					
Study ID	**Harrison 2013**					
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	18	4 wk treatment with homeopathic combination including a complex of 8 remedies ((1) Ambra grisea 6cH, (2) Arsenicum album 6cH, (3) Coffea cruda 6cH, (4) Delphinium staphisagria 6cH, (5) Ignatia amara 6cH, (6) Lycopodium clavatum 6cH, (7) Passiflora incarnata 6cH, and (8) Valeriana officinalis 6cH), sublingual administration, 5 drops before supper and before bed			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	16	Administered as per intervention			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison=control				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Pre-Sleep Arousal	Daily for 4 wks	Pre-Sleep Arousal Scale	16 questions organised into cognitive and somatic subscales. Participants completed each night before bed.	
2	Not specified	Sleep latency	Daily for 4 wks	Sleep diary	Length of time taken to fall asleep each night. Participants completed each morning.	
3	--	--	--	--	--	--
4	--	--	--	--	--	--
5	--	--	--	--	--	--
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--

Characteristics of included studies	INSOMNIA					
Study ID	**Harrison 2013**					
9	--	--	--	--	--	--
10	--	--	--	--	--	--
11	--	--	--	--	--	--
Method of analysis						
Statistics	Non-parametric Mann Whitney U tests for intergroup comparisons. Friedman test to compare results within groups and Wilcoxon signed-rank test to establish which wk the changes occurred.					
Population analysed	Per protocol	Per protocol interpreted. Participants 'lost to follow up' include those who did not comply with study procedures or who used insomnia medication.				
Missing data	Yes	6/34 (17.6%) dropped out of the study. These participants were excluded from the analysis with no attempt to account for missing data.				

Characteristics of included studies	INSOMNIA	
Study ID	**James 2019**	
Study reference	James M. Efficacy of individualized homeopathic treatment of insomnia: Double-blind, randomized, placebo-controlled clinical trial. Complementary Therapies in Medicine. 2019;43:53-9. CTRI/2017/05/008450	
Study design	RCT	Random number generator, block size of 10
Author affiliation	Homeopathic research institute in India	
Source of funds	No funding received	
Declared interests of study authors	The authors declared no conflict of interest	
Setting / provider	Outpatient, single centre	
Country(s) / region	India	
Enrolment period	May 2017 - June 2018	
Length of intervention + follow up	3 mth intervention, no follow up reported	
Description of population	*N=*	
participants	60	**Chronic insomnia**
details	Inclusion criteria: aged 18-65, suffering chronic insomnia, both male and female Exclusion criteria: uncontrolled illness or life-threatening infection, cases already undergoing homoeopathic treatment for any chronic disease, substance abuse, pregnant or lactating women, psychiatric diseases, self-reported immune compromised status	

Characteristics of included studies	INSOMNIA					
Study ID	**James 2019**					
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*			
Intervention #1	Individualised	30	3 mths treatment. individualised dosage as appropriate to the case or condition, dose to be taken orally on clean tongue with empty stomach, in centesimal or 50 millesimal potencies			
Intervention #2	--	--			--	
Comparator #1 (control)	Placebo	30	Placebo			
Comparator #2 (other)	--	--			--	
Comparator #3 (other)	--	--			--	
Co-interventions	All participants were encouraged to develop good sleep hygiene and habits					
Is comparator clearly inactive?	Yes	Comparison=control				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Sleep latency	Baseline, post intervention (3 mths)	Time to sleep onset	Sleep diary	
2	Primary	Awake time	Baseline, post intervention (3 mths)	Awake time during night	Sleep diary	
3	Primary	Difficulties maintaining sleep	Baseline, post intervention (3 mths)	Awake too early	Sleep diary	
4	Primary	Awake time	Baseline, post intervention (3 mths)	Hours spent in bed	Sleep diary	
5	Primary	Sleep duration	Baseline, post intervention (3 mths)	Total sleep time	Sleep diary	
6	Primary	Sleep efficiency	Baseline, post intervention (3 mths)	Not reported	Sleep diary	
7	Secondary	Insomnia severity	Baseline, post intervention (3 mths)	Insomnia Severity Index	Higher score is worse, total scores range 0-28	
8	--	--	--	--	--	--

Characteristics of included studies	INSOMNIA					
Study ID	**James 2019**					
9	--	--	--	--	--	--
10	--	--	--	--	--	--
11	--	--	--	--	--	--
Method of analysis						
Statistics	Group differences assessed using unpaired t test. P value of 0.01 was considered significant. No interim or subgroup analyses planned.					
Population analysed	Intent-to-treat	ITT is specified and conducted				
Missing data	Yes	Missing values replaced with regression means, last observation carried forward and multiple imputations using linear regression models.				

Characteristics of included studies	INSOMNIA
Study ID	**Jong 2016**
Study reference	Jong MC, Ilyenko L, Kholodova I, Verwer C, Burkart J, Weber S, et al. A Comparative Randomized Controlled Clinical Trial on the Effectiveness, Safety, and Tolerability of a Homeopathic Medicinal Product in Children with Sleep Disorders and Restlessness. Evidence-Based Complementary & Alternative Medicine: eCAM. 2016;2016:9539030. Jong C, Ilyenko L, Kholodova I, Verwer C, Burkart J, Weber S, et al. A comparative randomized controlled clinical trial on the effectiveness, safety, and tolerability of a homeopathic medicinal product in children with sleep disorders and restlessness. [Bulgarian]. Pediatriya. 2016;56(4):55-60. Burkart J, Jong MC, Ilenkyo L, Kholodova I, Verwer C, Weber S, et al. Results of a randomised controlled trial with a homeopathic complex medicinal product in children with sleep disorders and restlessness. Archives of Disease in Childhood. 2017;102(Supplement 2):A100-A1.
Study design	RCT Random code generated by external centre, sealed envelopes to conceal allocation
Author affiliation	Research institutes and universities in Netherlands, Sweden, Russia, and Germany
Source of funds	Study was sponsored by the Deutsche Homoopathie-Union, DHU-Arzneimittel GmbH & Co
Declared interests of study authors	Miek C. Jong was an employee of VSM Geneesmiddelen bv (sister-company of Deutsche Homoopathie-Union) from 2001 till 2008. Petra Klement and Julia Burkart are employees of Deutsche Homoopathie-Union, DHU-Arzneimittel GmbH & Co. KG, Karlsruhe, Germany. Stephan Weber and Thomas Keller received a fee from Deutsche Homoopathie-Union for their contribution in the statistical analysis.
Setting / provider	Outpatient, multicentre
Country(s) / region	Russia
Enrolment period	September 2010 - May 2011
Length of intervention + follow up	4 wk intervention, no follow up
Description of population	*N=*
participants	180 Children with **sleep disorders**
details	Inclusion criteria: children of both genders, up to 6 years old, sleep disorders which manifest in difficulty falling asleep and maintaining sleep, present for at least 1 mth prior to study start Exclusion criteria: sleep disorder associated with somatic or psychiatric illness, intracranial hypertension or severe concomitant disease (renal failure, heart anomalies, circulatory failure, cardiomyopathy, decompensated liver or kidney, immunosuppressive conditions, oncological diseases), known or suspected hypersensitivities to the study medications, participation in other clinical trials in past 6 mths, use of other medications with sedative, soporific or psychostimulant action within 30 days

Characteristics of included studies	INSOMNIA					
Study ID	**Jong 2016**					
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*			
Intervention #1	Non-individualised	90	4 wks, ZinCyp-3-02 (Cypripedium pubescens D4, Magnesium carbonicum D10, and Zincum valerianicum D12), one tablet x four times daily			
Intervention #2	--	--			--	
Comparator #1 (control)	--	--	--			
Comparator #2 (other)	Active control	90	Glycine tablets, one tablet x two times per day			
Comparator #3 (other)	--	--			--	
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison=control				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Sleep symptoms	Day 0, Day 3-5, Day 14, Day 28	Total complaints severity score (Higher is worse)	Parents report symptoms: total	
2	Secondary	Sleep latency	Day 0, Day 3-5, Day 14, Day 28	Time to sleep onset	Parent report: subscale	
3	Secondary	Sleep duration	Day 0, Day 3-5, Day 14, Day 28	Total sleep time	Parent report: subscale	
4	Secondary	Physical inactivity	Day 0, Day 3-5, Day 14, Day 28		Parent report: subscale	
5	Secondary	Slowness of movements	Day 0, Day 3-5, Day 14, Day 28		Parent report: subscale	
6	Secondary	Difficulties maintaining sleep	Day 0, Day 3-5, Day 14, Day 28		Parent report: subscale	
7	Secondary	Troubled sleep	Day 0, Day 3-5, Day 14, Day 28		Parent report: subscale	
8	Secondary	Restlessness	Day 0, Day 3-5, Day 14, Day 28		Parent report: subscale	

Characteristics of included studies	INSOMNIA				
Study ID	**Jong 2016**				
9	Secondary	Sleep disorders frequency	Day 0, Day 3-5, Day 14, Day 28		Parent report: subscale
10	Secondary	Sleep symptoms	Day 0, Day 3-5, Day 14, Day 28	5-point verbal scale	
11	Secondary	Treatment satisfaction	Day 28	5-point verbal scale	
Method of analysis					
Statistics	As primary analysis method, changes in total complaints severity scores were investigated by proportional odds model (POM) taking into account study specific situation of repeatedly measured outcome. Differences between treatment groups were presented as odds ratio (OR) estimates along with their two-sided 95% confidence intervals (CI) and related p values. All secondary outcome parameters were presented by descriptive statistics in counts and percentages. To test treatment related differences for all secondary outcome parameters, Chi-square tests were performed. A rejection criterion of 0.05 was set for all statistical tests.				
Population analysed	Intent-to-treat	ITT is specified. Only includes children who were randomised, received at least one dose of study medication and had one post-baseline result			
Missing data	No	4/180 (2.2%) participants did not complete the intervention period.			

Characteristics of included studies	INSOMNIA	
Study ID	**Naude 2010**	
Study reference	Naude DF, Stephanie Couchman IM, Maharaj A. Chronic primary insomnia: Efficacy of homeopathic simillimum. Homeopathy: the Journal of the Faculty of Homeopathy. 2010;99(1):63-8.	
Study design	quasi RCT	Numbers drawn from a hat, pre-determined randomisation sequence
Author affiliation	University in South Africa	
Source of funds	No information	
Declared interests of study authors	No information	
Setting / provider	Day clinic, single centre	
Country(s) / region	South Africa	
Enrolment period	Not reported	
Length of intervention + follow up	4 wk intervention, no follow up reported	
Description of population	*N=*	
participants	33	**Primary insomnia**
details	Inclusion criteria: Primary insomnia according to DSM4 criterion 307.42 Exclusion criteria: Use of additional sleep aids, interventions or medication	

Characteristics of included studies	INSOMNIA					
Study ID	**Naude 2010**					
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*			
Intervention #1	Individualised	16	4 wks, after discussion of each participant, the indicated homeopathic simillium was determined for each participant based on repetorisation of the totality of symptoms. The dosage was limited to three single-dose lactose powder sachets per consultation, one of which was dissolved sublingually each night consecutively before going to sleep. Participants were instructed to start taking the remedy on the eighth night after the initial consultation. After 2 wks, the homeopath could change or keep the remedy the same.			
Intervention #2	--	--			--	
Comparator #1 (control)	Placebo	17	Placebo, offered homeopathy post-intervention period			
Comparator #2 (other)	--	--			--	
Comparator #3 (other)	--	--			--	
Co-interventions	No further treatment was prescribed					
Is comparator clearly inactive?	Yes	Comparison=control				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Not specified	Time of retiring	Baseline, mid (wk 2), postintervention (wk 4)	Sleep diary		
2	Not specified	Time of arising	Baseline, mid (wk 2), postintervention (wk 4)	Sleep diary		
3	Not specified	Sleep duration	Baseline, mid (wk 2), postintervention (wk 4)	Total sleep time	Sleep diary	
4	Not specified	Difficulties maintaining sleep	Baseline, mid (wk 2), postintervention (wk 4)	Number of sleep interruptions	Sleep diary	
5	Not specified	Quality of sleep	Baseline, mid (wk 2), postintervention (wk 4)	Sleep diary	Sleep diary	
6	Not specified	Daytime naps	Baseline, mid (wk 2), postintervention (wk 4)	Sleep diary	Sleep diary	
7	Not specified	Sleep impairment	Baseline, mid (wk 2), postintervention (wk 4)	Sleep Impairment Index (Higher score is worse)	Perception of insomnia, severity, distress and impairment	
8	--	--	--	--	--	--

Characteristics of included studies	INSOMNIA					
Study ID	**Naude 2010**					
9	--	--	--	--	--	--
10	--	--	--	--	--	--
11	--	--	--	--	--	--
Method of analysis						
Statistics	Non-parametric tests due to small sample size and data not being normally distributed, p<0.05 considered significant. Data from the SII were analysed both per question and in the form of summary scores.					
Population analysed	Per protocol	Modified ITT interpreted, participants who did not complete follow up were excluded. One participant excluded due to non-compliance with medication instructions.				
Missing data	Yes	3/33 (9%) of participants did not complete follow up. No methods of adjustment reported. Loss to follow up was due to scheduling difficulties (n=2) and non compliance with treatment and measurement regime (n=1).				

Characteristics of included studies	HEADACHE		
Study ID	**Gaus 1992**		
Study reference	Walach H, Haeusler W, Lowes T, Mussbach D, Schamell U, Springer W, et al. Classical homeopathic treatment of chronic headaches. Cephalalgia. 1997;17(2):119-26.1. Walach H, Lowes T, Mussbach D, Schamell U, Springer W, Stritzl G, et al. The long-term effects of homeopathic treatment of chronic headaches: 1 Year follow up. Cephalalgia. 2000;20(9):835-7. 1. Gaus W. Biometrische Aspekte der 'Munchener Kopfschmerzstudie'. Allgemeine Homoopathische Zeitung. 1997;242(6):245-9. Gaus W, Walach H, Haag G. [The efficacy of classic homeopathic therapy in chronic headache. Study protocol.]. Der Schmerz. 1992;6(2):134-40.		
Study design	RCT	Homeopathic doctor choose single individual remedy for patient, selected remedy was mailed to a notary public with stock of placebos, notary through dic and mailed either homeopathic remedy or appropriate placebos	
Author affiliation	All authors from institutes in Germany		
Source of funds	Robert-Bosche-Foundation		
Declared interests of study authors	No information		
Setting / provider	Multi centre, patients recruited via ad in local newspaper in Munich		
Country(s) / region	Germany		
Enrolment period	October 1991 to October 1992		
Length of intervention + follow up	Baseline 6 wks, 12 wk treatment, 1 year follow up		
Description of population	*N=*	*Description*	
participants	98	Patient with headache	
details	*Inclusion criteria:* informed consent; headache for at least 1 year, at least once per wk; willingness to comply with possible dietary regimes advised by the homeopathic doctor *Exclusion criteria:* spinal trauma in last 4 years; life threatening diseases; and other serious conditions requiring treatment; abuse of alcohol; recreational drug and pharmaceutical drugs; psychiatric history, pregnancy or wish to become pregnant, foreseeable life events in the near future, medically necessary continuing medication which could interfere with homeopathic treatment, oral contraceptives, any contraindication to homeopathic treatment, impossibility to find homeopathic remedy. Post traumatic headaches excluded because creating physicians had no experience with this type of patients		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*
Intervention #1	Individualised	61	homeopathic doctor chose single individualised remedy for patient, either high centesimal (C) potency (dilution ration 1:100) distributed in single doses as sugar granules, or in a wuinquagesimillesimal (Q or LM) potency (dilution 1:50,000) distributed daily dose liquid form

Characteristics of included studies	HEADACHE		
Study ID	**Gaus 1992**		
Intervention #2		--	--
Comparator #1 (control)	Placebo	37	identical placebo gelatine capsule
Comparator #2 (other)		--	--
Comparator #3 (other)		--	--
Co-interventions	None reported		
Is comparator clearly inactive?	Yes	Comparison=control	

Characteristics of included studies	HEADACHE					
Study ID	**Gaus 1992**					
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Headache frequency	baseline (wks -4 to 0), post treatment (wks 8 to 12)	Patient diary, per day	higher is worse	
2	Primary	Headache duration	baseline (wks -4 to 0), post treatment (wks 8 to 12)	hours, Patient diary	higher is worse	
3	Primary	Headache pain intensity	baseline (wks -4 to 0), post treatment (wks 8 to 12)	100 mm VAS, per headache	higher is worse	
4	Secondary	Medication use	baseline (wks -4 to 0), post treatment (wks 8 to 12)	mg daily intake	higher is worse	
5	--	--	--	--	--	--
Method of analysis						
Statistics	Post minus pre treatment differences used. For hypothesis testing of primary outcome variables, non-parametric tests were considered with adjustment type 1 error with Holms correction for multiple testing					
Population analysed	Intent-to-treat	ITT specified, data from 6 drop-out included in analysis				
Missing data	Yes	98 randomised, four withdrawals in homeopathy group, two in placebo				

Characteristics of included studies	MIGRAINE		
Study ID	**Straumsheim 1997**		
Study reference	Straumsheim PA, Borchgrevink C, Mowinckel P, Kierulf H, Hafslund O. Homoeopathic treatment of migraine. A double-blind placebo controlled trial of 68 patients. Dynamis (Granada, Spain). 1997;2. Straumsheim P, Borchgrevink C, Mowinckel P, Kierulf H, Hafslund O. Homeopathic treatment of migraine: A double blind, placebo controlled trial of 68 patients. British Homeopathic Journal. 2000;89(1):4-7.		
Study design	RCT	patients were block-randomised into treatment or placebo group, stratified common (migraine without aura) or classical (migraine with aura) migraine. Homeopathic medicines and placebo bottles were coded by a statistician otherwise uninvolved in trial.	
Author affiliation	All authors from Arena Medisinske Senter, Norway		
Source of funds	Norwegian Research council		
Declared interests of study authors	No information		
Setting / provider	Single centre, Patients were recruited via St. Hansenhaugen MedicalCentre		
Country(s) / region	Norway		
Enrolment period	February 2006 to September 2008		
Length of intervention + follow up	One mth baseline registration, patients treated for 5 mths with consultation with homeopath every mth (to decide to continue, stop or change medicine)		
Description of population	*N=*	*Description*	
participants	68	patient with migraine	
details	*Inclusion criteria:* 18 to 65 years with migraine according to international headache society's classification criteria, diagnosed by a neurologist. Condition should have lasted at least one year, with a frequency of two to six attacks per mth over the preceding six mths *Exclusion criteria:* Pregnant and breast feeding women, patients using regular migraine preventative medicines, those with serious hypertension and users of benzodiazepines or hormonal preparations. Patients who abused stimulants or had an illness that made the practical participation in the trial difficult		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	35	All patients interviewed by homeopathic practitioner for between one and two hours. Potency and dose individually decided. Patients re-assessed every mth to decide whether patients continue, stop or change medicine.

Characteristics of included studies	MIGRAINE		
Study ID	**Straumsheim 1997**		
Intervention #2		--	--
Comparator #1 (control)	Placebo	33	Placebo in identical glass bottle to placebo
Comparator #2 (other)		--	--
Comparator #3 (other)		--	--
Co-interventions	None reported		
Is comparator clearly inactive?	Yes	Comparison=control	

Characteristics of included studies	MIGRAINE					
Study ID	**Straumsheim 1997**					
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Not specified	Average pain intensity	baseline, end of treatment (4 mths)	100-mm VAS, per attack	higher is worse	
2	Not specified	Frequency of attack	baseline, end of treatment (4 mths)	patient diary, attacks per mth	higher is worse	
3	Not specified	Frequency of attack	baseline, end of treatment (4 mths)	patient diary	Neurologist assessment of patient diary	
4	Not specified	Neurologist final evaluation	baseline, end of treatment (4 mths)	patient diary	Neurologist assessment of patient diary	
5	Not specified	Medication use	baseline, end of treatment (4 mths)	patient diary		
Method of analysis						
Statistics	Continuous variables were analysed with t-tests, and discrete with single Chi-square tests. Attack frequency per time unit was calculated and this variable was analysed with the help of repeated measures ANOVA. All P-values of 0.05 or less were considered significant. All the t-tests were two-tailed.					
Population analysed	Intent-to-treat	modified intent to treat - only analysed patients who completed trial				
Missing data	Yes	73 included, 1 excluded no migraine in mth before treatment, two pregnant, 1 hypertension, 1 lost to follow up. Not clear if excluded prior to randomisation.				

Characteristics of included studies	MIGRAINE		
Study ID	**Whitmarsh 1997**		
Study reference	Whitmarsh TE, Coleston-Shields DM, Steiner TJ. Double-blind randomized placebo-controlled study of homoeopathic prophylaxis of migraine. Cephalalgia. 1997;17(5):600-4.		
Study design	quasi RCT	cluster design	randomised within diagnostic group (with/ without aura) details of randomisation not specified
Author affiliation	The Princess Margaret Migraine clinic, London		
Source of funds	Homeopathic Medical Research council		
Declared interests of study authors	No information		
Setting / provider	Single centre, outpatient		
Country(s) / region	England		
Enrolment period	No information		
Length of intervention + follow up	1 mth baseline, 3 mth treatment		
Description of population	*N=*	*Description*	
participants	63	Patient with migraine	
details	Inclusion criteria: define diagnosis of migraine with or without aura by HIS criteria; recognisable attacks for at least the last two years; attack frequency b/w 2-8 per mth in each of the past 3 mths; age 18-60 yrs; informed consent Exclusion criteria: Symptoms not conforming to the prescribing criteria for any of 11 homeopathic remedies; other headaches more troublesome than migraine, or other cause of chronic/ recurrent pain; other illnesses requiring drug therapy; ovary depression; use of specific migraine prophylactics in the 2 mths prior to entry; change in use of oral contraceptives in previous 6 mo; pregnancy; inability to cooperate; entry to more that 2 clinical trial previously		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*
Intervention #1	Individualised	32	11 homeopathic remedies available, selected on advice of homeopathic physician - Belladonna, Bryonia, Iris versicolor, Kali bichromatum, Lachesis, Natrim muriaticum, Nux vomica, Sanuinaria, Sepia, Silica and Sulphur - standard potency 30C, dosing regimen two tablets twice a wk

Characteristics of included studies	MIGRAINE		
Study ID	**Whitmarsh 1997**		
Intervention #2		--	--
Comparator #1 (control)	Placebo	31	Identical placebo
Comparator #2 (other)		--	--
Comparator #3 (other)		--	--
Co-interventions	None reported		
Is comparator clearly inactive?	Yes	Comparison=control	

Characteristics of included studies	MIGRAINE					
Study ID	**Whitmarsh 1997**					
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Not specified	Migraine attack frequency	baseline, mthly, end of treatment (4 mths)	patient diary	migraine frequency over trial period, higher is worse	
2	Not specified	Migraine severity	baseline, mthly, end of treatment (4 mths)	Patient reported scale	(mild, moderate, severe)	
3	Not specified	treatment efficacy	baseline, mthly, end of treatment (4 mths)	patient report scale	(good, moderate, none)	
4	Not specified	Side effects	baseline, mthly, end of treatment (4 mths)	patient reported scale	(unacceptable, acceptable, none)	
5	--	--	--	--	--	
Method of analysis						
Statistics	A difference in treatment groups of 1.5 attacks per mth was taken to be statistically significant, no statistical analysis performed					
Population analysed	Per protocol	Drop outs not included in analysis				
Missing data	Yes	three drop out (4.8%), 1 failed to attend 2nd mth, 1 lung tumour, 1 commenced opioid analgesia, one felt not worthwhile continuing				

Characteristics of included studies	Asthma, allergic	
Study ID	**Lewith 2002**	
Study reference	Lewith GT, Watkins AD, Hyland ME, Shaw S, Broomfield JA, Dolan G, et al. Use of ultramolecular potencies of allergen to treat asthmatic people allergic to house dust mite: Double blind randomised controlled clinical trial. British Medical Journal. 2002;324(7336):520-3.	
Study design	RCT	randomised the first 10 participants to treatment A or to B using a sealed envelope. All subse-quent participants were allocated to A or B by a proc-ess of minimisation according to age, sex, smoking status, severity of asthma
Author affiliation	Authors were affiliated with a hospital and university in the UK	
Source of funds	The study was funded by Smith's Charity, NHS Executive South and West Research and Development Directorate, Boiron. The authors' post was funded by a grant from the Maurice Laing Foundation.	
Declared interests of study authors	The authors declared no conflict of interest	
Setting / provider	Multicentre - 38 general practices in Hampshire and Dorset, UK	
Country(s) / region	Hampshire and Dorset, England, UK	
Enrolment period	September to April 2001	
Length of intervention + follow up	16 wk intervention	
Description of population	*N=*	*Description*
participants	242	Allergic asthma (dust mites)

Characteristics of included studies	Asthma, allergic					
Study ID	**Lewith 2002**					
details	Inclusion criteria: positive result to house dust mite (wheal diameter 3 mm greater than negative control 15 min after test), 15% improvement in forced expiratory volume in one second or peak expiratory flow 15 minutes after a 200 ìg inhalation of salbutamol before randomisation and two of three criteria of an asthma symptom diary score of > 1 on at least seven of the 14 baseline days during the run-in period or a diurnal variation in peak expiratory flow of > 15% on at least seven of the 14 baseline days or a need for inhaled salbutamol on at least seven of the 14 baseline days. Exclusion criteria: Patients record no impairment in quality of life in diaries during run-in period or if they filled in diaries on fewer than 10 days during that period. Patients who had taken part in another drug trial within the previous 30 days, had previously been treated with homeopathic immunotherapy, were pregnant or lactating, were unlikely to comply with trial requirements, had respiratory tract infection within the last three wks or changed there concurrent medication in the two wks before entry					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Non-individualised	122	Ultramolecular dose of house dust mite as a 30C potency, taken orally on 3 occasions over 24 hours			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	120	Identical dilution without house dust mite, taken orally on 3 occasions over 24 hours			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Concurrent medications remained unchanged					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Pulmonary function	Baseline, 6, 12 and 16 wks post randomisation	Forced expiratory volume in first second	higher is better mean change from baseline	

Characteristics of included studies	Asthma, allergic					
Study ID	**Lewith 2002**					
2	Secondary	Pulmonary function	Baseline and every second wk until end of treatment (16 wks)	Peak expiratory flow	Higher is better	
3	Secondary	Asthma symptom severity	Baseline and every second wk until end of treatment (16 wks)	Visual analogue scale	Higher is worse	
4	Secondary	Asthma symptoms	Baseline and every second wk until end of treatment (16 wks)	Proportion of symptom free days	Higher is better	
5	Secondary	Perceived mood	Baseline and every second wk until end of treatment (16 wks)	Bipolar mood scale	Higher is better	
6	Secondary	Medication use	Baseline and every second wk until end of treatment (16 wks)	Frequency of daily use (of prescribed bronchodilator)	Higher is worse	
7	Secondary	Quality of life	Baseline, 6, 12 and 16 wks post randomisation	Asthma bother profile	Higher is worse	
8	Primary	Quality of life	Baseline and every second wk until end of treatment (16 wks)	Proportion of days when no problems were reported in 6 categories	Categories not specified	
9	--	--	--	--	--	--
10	--	--	--	--	--	--
11	--	--	--	--	--	--
12	--	--	--	--	--	--
13	--	--	--	--	--	--
14	--	--	--	--	--	--
15	--	--	--	--	--	--

Characteristics of included studies	Asthma, allergic	
Study ID	**Lewith 2002**	
Method of analysis		
Statistics	Authors examined all outcome measures for suitability for parametric analysis. tested blinding with X^2 test. Tested clinical efficacy by comparing the two treatment groups at the end of the study (wk 16 for clinic assessments and wk 15 for diary assessments) using analysis of covariance. For FEV1 the covariate was the average assessment at the start and end of the run-in period. For the other clinic based outcomes the covariate was the value obtained at the start of the run-in period. For outcome measures assessed from diaries the covariate was the value obtained from the average of values during the run-in period.	
Population analysed	Intent-to-treat	
Missing data	Yes	40/242 participants withdrew from the study

Characteristics of included studies	Asthma, bronchial	
Study ID	**Qutubuddin 2019**	
Study reference	Qutubuddin M, Murty Singh S, Nayak C, Koley M, Saha S. Efficacy of individualized homeopathy in bronchial asthma in adults: Double-blind, randomized, placebo-controlled, clinical trial in the context of usual care. Advances in Integrative Medicine. 2019;6(2):58-65. CTRI/2017/08/009192	
Study design	RCT	Computer generated random numbers. Allocation concealment managed by a third party
Author affiliation	Authors were affiliated with a hospital, university, research centre and council of homeopathy located in India	
Source of funds	Authors declared they did not receive funding for the project, and the affiliated institution had no role to play in the study and publication of the paper	
Declared interests of study authors	The authors declared no conflict of interest	
Setting / provider	Outpatient clinic	
Country(s) / region	Darbhanga, India	
Enrolment period	January 2014 to June 2017	
Length of intervention + follow up	6 mth intervention, results measured at 3 and 6 mths	
Description of population	*N=*	*Description*
participants	140	Adults with asthma

Characteristics of included studies	Asthma, bronchial					
Study ID	**Qutubuddin 2019**					
details	Inclusion criteria: Aged between 18-65, both sexes, ability to read Hindi and consenting to participant, diagnosed persistent bronchial asthma (mild to moderate), typical regular asthmatic attacks and illness persisting for 1 year or longer. Exclusion criteria: Too unwell to take part, respiratory tract infection in the past 3 wks, other diseases causing pulmonary obstruction, other uncontrolled pulmonary or systemic diseases, psychiatric illness, pregnancy or lactation, previous immunotherapy, ongoing use of homeopathic remedies for chronic purpose, any change in concurrent medication in the 2 wks prior to entry, substance abuse, and unwillingness to participate or comply with trial requirements.					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Individualised	70	Participants were assessed by a homeopath and prescribed single individualised homeopathy taken orally at 24, 12 or 8 hour intervals. Duration of treatment was 6 mths			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	70	Participants were assessed by a homeopath and dispensed a placebo consisting of cane sugar and a rectified spirit, taken orally 3 times per day. Duration of treatment was 6 mths			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Usual care, which consisted of β agonists, corticosteroids, antihistamines, montelukasts, etc. along with oral short-acting bronchodilators and breathing exercises					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis		Placebo		
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Pulmonary function	Baseline, interim (3 mths), end of treatment (6 mths)	Forced expiratory volume in first second	Higher is better	

Characteristics of included studies	Asthma, bronchial				
Study ID	**Qutubuddin 2019**				
2	Primary	Pulmonary function	Baseline, interim (3 mths), end of treatment (6 mths)	Forced vital capacity	Higher is better
3	Primary	Pulmonary function	Baseline, interim (3 mths), end of treatment (6 mths)	Forced expiratory volume in first second / Forced vital capacity	Higher is better
4	Primary	Pulmonary function	Baseline, interim (3 mths), end of treatment (6 mths)	Forced expiratory flow	Higher is better
5	Primary	Pulmonary function	Baseline, interim (3 mths), end of treatment (6 mths)	Peak expiratory flow	Higher is better
6	Primary	Immune function	Baseline, interim (3 mths), end of treatment (6 mths)	Blood eosinophil percentage	Below 7% is considered normal
7	Primary	Immune function	Baseline, interim (3 mths), end of treatment (6 mths)	Serum immunoglobulin E (IgE; IU/ml)	Below 300 UI/mL is considered normal
8	Secondary	Asthma symptoms	Baseline, interim (3 mths), end of treatment (6 mths)	Number of attacks last wk	Higher is worse
9	Secondary	Asthma symptoms	Baseline, interim (3 mths), end of treatment (6 mths)	Days of symptoms last wk	Higher is worse
10	Secondary	Asthma symptoms	Baseline, interim (3 mths), end of treatment (6 mths)	Average sleep interference last wk (hrs/day)	Higher is worse
11	Secondary	Asthma symptoms	Baseline, interim (3 mths), end of treatment (6 mths)	Frequency of bronchodilator use last wk	Higher is worse
12	Secondary	Asthma symptoms	Baseline, interim (3 mths), end of treatment (6 mths)	NRS - severity	Range: 0-10 Higher is worse
13	Secondary	Asthma symptoms	Baseline, interim (3 mths), end of treatment (6 mths)	NRS - global wellbeing	Range: 0-10 Higher is worse
14	Secondary	Asthma symptoms	Baseline, interim (3 mths), end of treatment (6 mths)	Asthma control questionnaire (ACQ)	Range: 0-6 Higher is worse
15	Secondary	Asthma symptoms	Baseline, interim (3 mths), end of treatment (6 mths)	Asthma control test (ACT)	Range: 1-25 Higher is better

Characteristics of included studies	Asthma, bronchial	
Study ID	**Qutubuddin 2019**	
Method of analysis		
Statistics	Groups were checked for comparability at baseline using independent t-tests or chi-squared tests. Group differences were tested by independent t-test	
Population analysed	Intent-to-treat	ITT specified and conducted
Missing data	Yes	18/140 participants withdrew from the study. Missing values were replaced by last value carried forward method and the ITT sample was analysed

Characteristics of included studies	Asthma, allergic	
Study ID	**Reilly 1994**	
Study reference	Reilly D, Taylor M, Beattie N, Campbell J, McSharry C, Aitchison T, et al. Is evidence for homoeopathy reproducible? Lancet. 1994;344(8937):1601-6.	
Study design	RCT	Permuted block randomisation stratified for the indicated allergen and daily dosage of inhaled steroid. Pharmacist had access to the code which was not broken until after analysis
Author affiliation	Authors were affiliated with universities in the UK	
Source of funds	The Blackie Foundation Trust and Foundation Francaise pour la Recherche en Homeopathie provided grant aided support for this study	
Declared interests of study authors	Not reported	
Setting / provider	Outpatient clinics	
Country(s) / region	West-central Scotland	
Enrolment period	Not reported	
Length of intervention + follow up	4 wk intervention with option to complete an additional 4 wks. Results reported at 4 wks, additional results reported at 8 wks	
Description of population	*N=*	*Description*
participants	28	Allergic asthma

Characteristics of included studies	Asthma, allergic					
Study ID	**Reilly 1994**					
details	Inclusion criteria: Aged over 16 years, greater than 1 year history of asthma, greater than 15% improvement in FEV1 with bronchodilators, reactive to inhaled allergens and positive skin tests Exclusion criteria: Deterioration during grass-pollen season, allergen avoidance within previous 6 wks, previous homeopathic immunotherapy for asthma, respiratory infection, severe concomitant disease, pregnancy, antihistamines use in past 4 wks, parenteral steroid use in past 6 mths					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Individualised	13	Participants were assessed at baseline and prescribed a homeopathic treatment based on their principle allergen. Treatment contained 3 vials taken orally within 24 hours (on the same day as treatment allocation)			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	15	Participants allocated to placebo were also assessed by a homeopath and received an identical placebo taken orally within 24 hours on the same day as treatment allocation			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Usual care					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptom severity	Daily, up to 4 wks	Visual analogue score (VAS) (0-100mm)	"Overall today I felt ...", (fine... terrible) intent the scale was about asthma, but the wording may include some element of general well being.	

Characteristics of included studies	Asthma, allergic					
Study ID	**Reilly 1994**					
2	Secondary	Pulmonary function	Baseline and 4 wks	Forced expiratory volume in first second	Higher is better	
3	Secondary	Pulmonary function	Baseline and 4 wks	FVC	Higher is better	
4	Secondary	Pulmonary function	Baseline and 4 wks	Methacholine (PC20) test	PD20 <1000 µg is of concern	
5	--	--	--	--	--	--
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--
9	--	--	--	--	--	--
10	--	--	--	--	--	--
11	--	--	--	--	--	--
12	--	--	--	--	--	--
13	--	--	--	--	--	--
14	--	--	--	--	--	--
15	--	--	--	--	--	--

Characteristics of included studies	Asthma, allergic	
Study ID	**Reilly 1994**	
Method of analysis		
Statistics	Two-tailed two-sample t tests were applied to data with normal distributions and Mann-Whitney U tests on skewed data. Chi squared tests and McNemar's test of symmetry were applied where appropriate. Analysis performed by independent statistician	
Population analysed	Intent-to-treat	ITT specified and conducted
Missing data	Yes	4/28 participants withdrew from the study

Characteristics of included studies	Asthma, bronchial	
Study ID	**Thompson 2008**	
Study reference	Thompson EA, Shaw A, Nichol J, Hollinghurst S, Henderson AJ, Thompson T, et al. The feasibility of a pragmatic randomised controlled trial to compare usual care with usual care plus individualised homeopathy, in children requiring secondary care for asthma. Homeopathy: the Journal of the Faculty of Homeopathy. 2011;100(3):122-30.	
Study design	quasi RCT	Patients were randomised to homeopathic treatment or usual care. Method of randomisation not specified
Author affiliation	Authors were affiliated with universities and a homeopathic hospital in the UK	
Source of funds	The study was funded by the Avon Primary Care Research Collaborative	
Declared interests of study authors	Not reported	
Setting / provider	Outpatient clinics	
Country(s) / region	Bristol, UK	
Enrolment period	1 January 2005 to 30 September 2007	
Length of intervention + follow up	16 wk intervention. Results measured at 4, 8, 12 and 16 wks	
Description of population	*N=*	*Description*
participants	39	Children with asthma

Characteristics of included studies	Asthma, bronchial					
Study ID	**Thompson 2008**					
details	Inclusion criteria: Aged 7-14 years, visited a secondary care respiratory clinic (the outpatient departments of the Bristol Royal Hospital for Children and Southmead Hospital, Bristol) and who were at Step 2 or above on the British Thoracic treatment steps Exclusion criteria: Presently using homeopathy, too unwell to take part or refused informed consent					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Individualised	18	Participants attended one long initial consultation with a homeopath, followed by 4 follow up visits spaced between 4-8 wks apart. Individualised oral homeopathic treatments were prescribed for a duration of 16 wks			
Intervention #2	--	--	--			
Comparator #1 (control)	Inactive control	21	Control (no intervention). Children in the control arm were seen at intervals appropriate to their needs as judged by the individual respiratory clinician who was not directly informed of randomisation status			
Comparator #2 (other)	--	--	--	--	--	--
Comparator #3 (other)	--	--	--	--	--	--
Co-interventions	Usual care					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Control (no intervention)	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Asthma symptoms	Baseline, 4, 8, 12, 16 wks	Asthma control questionnaire	Range: 0-6 Lower is better	

Characteristics of included studies	Asthma, bronchial				
Study ID	**Thompson 2008**				
2	Secondary	Asthma symptoms	Baseline, 4, 8, 12, 16 wks	Paediatric AQLQ - symptoms domain	Rage: 1-7 Higher is better
3	Secondary	Asthma symptoms	Baseline, 4, 8, 12, 16 wks	Paediatric AQLQ - activity domain	Rage: 1-7 Higher is better
4	Secondary	Asthma symptoms	Baseline, 4, 8, 12, 16 wks	Paediatric AQLQ - emotional domain	Rage: 1-7 Higher is better
5	Secondary	Asthma symptoms	Baseline, 4, 8, 12, 16 wks	Interference with sleep	Lower is better
6	Secondary	Asthma symptoms	Baseline, 4, 8, 12, 16 wks	Days of symptoms	Lower is better
7	Secondary	Asthma symptoms	Baseline, 4, 8, 12, 16 wks	Interference with activities	Lower is better
8	Secondary	Pulmonary function	Baseline, 4, 8, 12, 16 wks	Peak flow (morning)	Higher is better
9	Secondary	Pulmonary function	Baseline, 4, 8, 12, 16 wks	Peak flow (evening)	Higher is better
10	Secondary	Medication use	Baseline, 4, 8, 12, 16 wks	Doses per wk on medication control questionnaire	Lower is better
11	Secondary	Medication use	Baseline, 4, 8, 12, 16 wks	Mean number of medications on medication control questionnaire	Lower is better
12	Secondary	Quality of life	End of treatment (16 wks)	Outcome in relation to daily living	Higher is better
13	--	Resource use	Study duration	Primary care/outpatient appointments	--
14	--	Resource use	Study duration	Inpatient stays	--
15	--	Resource use	Study duration	Days off work	--

Characteristics of included studies	Asthma, bronchial	
Study ID	**Thompson 2008**	
Method of analysis		
Statistics	Between group differences at follow up for each of the outcome measures were estimated using appropriate regression models, adjusting for minimisation variables and the value of the outcome variable at baseline.	
Population analysed	Intent-to-treat	ITT specified and conducted
Missing data	Yes	4/39 participants withdrew from the study

Characteristics of included studies	Asthma, bronchial	
Study ID	**Topcu 2010**	
Study reference	Topcu A, Lokke A, Eriksen L, Nielsen LP, Dahl R. Evaluating the effect on asthma quality of life of added reflexology or homeopathy to conventional asthma management–an investigator-blinded, randomised, controlled parallel group study. European Clinical Respiratory Journal. 2020;7(1). Topcu A, Ottesen AL, Eriksen L, Nielsen LP, Dahl R. The Impact of Reflexology and Homeopathy Added to Conventional ASTHMA Treatment on Markers of Airway Inflammation - A Randomised Study. European Respiratory Journal Conference: European Respiratory Society International Congress, ERS. 2020;56(Supplement 64). Topcu A, Lokke Ottesen A, Eriksen L, Nielsen LP, Dahl R. The impact of reflexology and homeopathy added to conventional asthma treatment on markers of airway inflammation - a randomised study. European Clinical Respiratory Journal. 2020;7(1).	
Study design	RCT	Computer generated random numbers. Treatment allocation codes given to patients by staff not otherwise involved in the study
Author affiliation	Authors were affiliated with hospitals, universities and the Danish National board of Health's Council Concerning Alternative Treatment and Reflexology in Denmark	
Source of funds	The study was funded by the Knowledge and Research Centre for Alternative Medicine, Denmark	
Declared interests of study authors	The authors declared no conflict of interest	
Setting / provider	Outpatient clinic	
Country(s) / region	Denmark	
Enrolment period	Not reported	
Length of intervention + follow up	52 wk intervention, results measured at 26 and 52 wks	
Description of population	*N=*	*Description*
participants	84	Adults with bronchial asthma

Characteristics of included studies	Asthma, bronchial					
Study ID	**Topcu 2010**					
details	Inclusion criteria: History of bronchial asthma for at least 6 mths prior to baseline, forced expiratory volume in 1 second ≥ 60% predicted before bronchodilator and an objective measure of abnormal variation in bronchial calibre. Exclusion criteria: Hospitalised for asthma within the past 3 mths or asthma exacerbation during the last mth, changes in asthma medication within 30 days from screening, smoking history >10 pack-years.					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Individualised	23	Participants attended 6 to 12 sessions with a homeopath and were prescribed individualised homeopathy treatments. Duration of treatment was 52 wks			
Intervention #2	Individualised	32	Participants received individualised reflexology, the number of sessions and duration of treatment was decided on an individual basis by the reflexologist			
Comparator #1 (control)	Inactive control	29	Control (no intervention)			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Usual care. All patients received usual care of asthma from their general practitioner who monitored and adjusted treatment during the study period					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis		Control (no intervention)		
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Quality of life	Baseline, interim (26 wks), end of treatment (52 wks)	Asthma quality of life questionnaire (AQLQ)	Range: 1-7 Higher is better	

Characteristics of included studies	Asthma, bronchial				
Study ID	**Topcu 2010**				
2	Secondary	Quality of life	Baseline, interim (26 wks), end of treatment (52 wks)	EQ-5D index	Range: 0-100 Higher is better
3	Secondary	Quality of life	Baseline, interim (26 wks), end of treatment (52 wks)	EQ-5D VAS	Range: 0-100 Higher is worse
4	Secondary	Pulmonary function	Baseline, interim (26 wks), end of treatment (52 wks)	Morning PEF	Higher is better
5	Secondary	Pulmonary function	Baseline, interim (26 wks), end of treatment (52 wks)	Evening PEF	Higher is better
6	Secondary	Pulmonary function	Baseline, interim (26 wks), end of treatment (52 wks)	Forced expiratory volume in first second	Higher is better
7	Secondary	Pulmonary function	Baseline, interim (26 wks), end of treatment (52 wks)	Exhaled nitric oxide	Results >50 ppb are considered high
8	Secondary	Pulmonary function	Baseline, interim (26 wks), end of treatment (52 wks)	Forced vital capacity	Higher is better
9	Secondary	Asthma symptoms	Baseline, interim (26 wks), end of treatment (52 wks)	Daytime asthma symptoms	Range: 0-5 Higher is worse
10	Secondary	Asthma symptoms	Baseline, interim (26 wks), end of treatment (52 wks)	Nocturnal asthma symptoms	Range: 0-5 Higher is worse
11	Secondary	Asthma symptoms	Baseline, interim (26 wks), end of treatment (52 wks)	Asthma control questionnaire (ACQ)	Range: 0-6 Higher is worse
12	Secondary	Immune function	Baseline, interim (26 wks), end of treatment (52 wks)	Serum eosinophil cationic protein	Normal range between 2.3 -16µg/L.
13	Secondary	Immune function	Baseline, interim (26 wks), end of treatment (52 wks)	Blood eosinophil count	Lower is better
14	Secondary	Medication use	Baseline, interim (26 wks), end of treatment (52 wks)	Rescue medication use	Higher is worse
15	Secondary	Medication use	Baseline, interim (26 wks), end of treatment (52 wks)	Total medication use	Higher is worse

Characteristics of included studies	Asthma, bronchial	
Study ID	**Topcu 2010**	
Method of analysis		
Statistics	Data were presented as mean (CI) when variables were normally distributed. Variables with skewed distribution were log transformed and reported as geometric means and CI. ANOVA model was used to estimate treatment group means and between-group differences	
Population analysed	Intent-to-treat	ITT specified and conducted
Missing data	Yes	14/84 participants did not complete the study. Missing values were imputed using last observation carried forward method and the ITT sample was analysed

Characteristics of included studies	Asthma, bronchial	
Study ID	**White 2003**	
Study reference	White A, Slade P, Hunt C, Hart A, Ernst E. Individualised homeopathy as an adjunct in the treatment of childhood asthma: A randomised placebo controlled trial. Thorax. 2003;58(4):317-21.	
Study design	RCT	Computer generated random numbers. Patients, homeopaths and research staff blinded to randomisation, code was not broken until data was analysed
Author affiliation	Authors were affiliated with universities and private practices in the UK	
Source of funds	The study was funded by the Prince of Wale's Foundation for Integrated Health, London	
Declared interests of study authors	The authors declared no conflict of interest	
Setting / provider	General practice clinics	
Country(s) / region	Somerset, UK	
Enrolment period	October 1997 to March 1999	
Length of intervention + follow up	52 wk intervention, results measured at 52 wks	
Description of population	*N=*	*Description*
participants	93	Children with mild to moderate asthma

Characteristics of included studies	Asthma, bronchial					
Study ID	**White 2003**					
details	Inclusion criteria: Children aged 5-15 years with mild to moderate asthma Exclusion criteria: Prescribed oral corticosteroids for acute asthma within the past 12 mths, previous homeopathic consultation and prescription, unable to comply with study requirements					
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*			
Intervention #1	Individualised	46	Participants could attend up to six homeopathic consultations over the study period with additional phone consultations as necessary. Participants were prescribed individualised homeopathy treatments for a duration of 12 mths			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	47	Placebo was dispensed by homeopathic pharmacist in identical form to the genuine treatment			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Usual care					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Placebo			
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Quality of life	Baseline and end of treatment (12 mths)	Childhood asthma questionnaire (CAQ) - active quality of living domain	Range: 0-100 Higher is better	

Characteristics of included studies	Asthma, bronchial				
Study ID	**White 2003**				
2	Secondary	Pulmonary function	Baseline and end of treatment (12 mths)	Improvement in PEFR	Reported binary outcomes (<15%, ≥15%) end of treatment compared to baseline
3	Secondary	Medication use	Baseline and end of treatment (12 mths)	Use of inhalers	Reported ordinal variables (increased, no change, reduced) end of treatment compared to baseline
4	Secondary	Asthma severity	Baseline and end of treatment (12 mths)	Days off school in past mth	Reported ordinal variables (increased, no change, reduced) end of treatment compared to baseline
5	--	--	--	--	--
6	--	--	--	--	--
7	--	--	--	--	--
8	--	--	--	--	--
9	--	--	--	--	--
10	--	--	--	--	--
11	--	--	--	--	--
12	--	--	--	--	--
13	--	--	--	--	--
14	--	--	--	--	--
15	--	--	--	--	--

Characteristics of included studies	Asthma, bronchial	
Study ID	**White 2003**	
Method of analysis		
Statistics	Changes in quality of life scores were analysed using analysis of covariance. Active quality of life scores and severity score data were pooled by converting scored into standardised values. Analysis was by intention to treat. Possible clustering effects investigated by adding random factor in Proc mixed using SAS. Time until asthma events or times between events were analysed by the Wilcoxon test using strata for the baseline severity with the STS test procedure in Intercooled Stata.	
Population analysed	Intent-to-treat	ITT specified and conducted
Missing data	Yes	19/93 participants did not complete the final questionnaire. Missing results were managed by carrying forward the baseline value - that is, 'no change'

Characteristics of included studies	DIARRHOEA		
Study ID	Jacobs 1993		
Study reference	Jacobs J, Jiminez L, Gloyd S, Carares F, Gaitan M, Crothers D. Homoeopathic treatment of acute childhood diarrhoea. Br Homoeopath J. 1993;82(2):83-6.		
Study design	Quasi-RCT		Not specified
Author affiliation	Two authors from American universities; one author from a Mexican university; two authors from a Nicaraguan university; one author from a homeopathic treatment centre in America		
Source of funds	Financially supported by Boiron Research Foundation, Norwood, Pennsylvania, USA		
Declared interests of study authors	No information		
Setting / provider	Community (home visits carried out by community health workers)		
Country(s) / region	Nicaragua		
Enrolment period	Jul-90		
Length of intervention + follow up	Intervention up to 3 days. Follow up for 6 days. (Until symptoms resolved).		
Description of population	*N=*	*Description*	
participants	34	Acute childhood diarrhoea	
details	Inclusion: Children aged 6 mths to 5 years with a history of acute diarrhoea. Exclusion: Children with a history of diarrhoea for more than 10 days or who had received anti-diarrhoeal medication within the previous 24 hours.		
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	16	Individualised homeopathic medicine, given in 30c potency on premedicated sucrose/lactose pellets, with one does to be taken twice daily for up to 3 days
Intervention #2			

Characteristics of included studies	DIARRHOEA					
Study ID	Jacobs 1993					
Comparator #1 (control)	Placebo	17	Administered as per intervention			
Comparator #2 (other) Comparator #3 (other)						
Co-interventions	Oral rehydration therapy according to WHO protocols					
Is comparator clearly inactive?	Yes	Comparison=control				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Mean duration of diarrhoea following intervention	6 days	Parent's recall of the number of loose stools	Duration defined as number of days following entry into the study until there were 2 consecutive days with less than 3 liquid bowel movements per day	
2	Not specified	Number of days to first diarrhoea-free day	6 days	Parent's recall of the number of loose stools	Fewer days is better	
3	Not specified	Symptom duration	6 days	Total number of days of diarrhoea	Parent's recall of the number of loose stools	Fewer days is better
4	Not specified	Symptom severity	6 days	Number of stools per day	Parent's recall of the number of loose stools	Fewer stools is better
5	Not specified	Weight gain (or loss)	6 days	Health worker evaluation and reweigh of child	Less weight loss is better	
NOTE:	Acute diarrhoea was defined as the passage of three or more liquid stools during the previous 24 hours					
Method of analysis						

Characteristics of included studies	DIARRHOEA	
Study ID	Jacobs 1993	
Statistics	2-sample, 2-tailed t-test to compare the descriptive characteristics at the initial visit between 2 groups and number of stools per day. Log rank test to compare duration of diarrhoea.	
Population analysed	Intent-to-treat	Modified ITT. One participant was randomised, but not included in analysis. Details not specified.
Missing data	Yes	One participant was randomised, but not included in analysis. Details not specified.

Characteristics of included studies	DIARRHOEA		
Study ID	Jacobs 2000		
Study reference	Jacobs, J., Jimenez, L. M., Malthouse, S., Chapman, E., Crothers, D., Masuk, M., & Jonas, W. B. (2000). Homeopathic treatment of acute childhood diarrhea: results from a clinical trial in Nepal [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. Journal of Alternative & Complementary Medicine, 6(2), 131-139.		
Study design	RCT	Random numbers table	
Author affiliation	Two author from American universities; one author from a Mexican university; two authors from a Nepalese university; one author from a homeopathic treatment centre in American; one author from America		
Source of funds	Research grant from Boiron Research Foundation, Norwood, Pennsylvania, USA		
Declared interests of study authors	No information		
Setting / provider	Private, charitable health clinic in Kathmandu, Nepal		
Country(s) / region	Nepal		
Enrolment period	April 25 1994 to June 25 1994		
Length of intervention + follow up	Intervention up to 5 days. Follow up for up to 5 days. (Until symptoms resolved).		
Description of population	*N=*	*Description*	
participants	126	Acute childhood diarrhoea	
details	Inclusion: Children aged 6 mths to 5 years with a history of diarrhoea (more than three unformed stools per day) for no more than 5 days. Exclusion: Children with a history of diarrhoea for more than 10 days or who had received anti-diarrhoeal medication within the previous 48 hours, children who had severe diarrhoea requiring hospitalisation or intravenous hydration.		
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*
Intervention #1	Individualised	69	Individualised homeopathic medicine, given in 30c potency via sucrose/lactose pellets, with one dose to be taken after each unformed stool for up to 5 days.
Intervention #2			

Characteristics of included studies	DIARRHOEA					
Study ID	Jacobs 2000					
Comparator #1 (control)	Placebo	57	Administered as per intervention			
Comparator #2 (other)						
Comparator #3 (other)						
Co-interventions	Oral rehydration therapy according to WHO protocols. Children found to have parasites were treated with standard antiparasitic medication at the end of the 5-day treatment period.					
Is comparator clearly inactive?	Yes	Comparison=control				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptom duration	Probability of being diarrhoea free in 5 days	Duration of diarrhoea	Parent's record of daily stools on diary cards	Time until there were two consecutive days with fewer than three unformed stools.
2	Not specified	Symptom severity	Up to 5 days	Average number of stools per day	Parent's record of daily stools on diary cards	Fewer stools is better
3	--	--				
4	--	--				
5	--	--				
NOTE:	--	--				
Method of analysis						

Characteristics of included studies	DIARRHOEA	
Study ID	Jacobs 2000	
Statistics	Kaplan-Meier plot used to compare duration of diarrhea; log-rank test of the Kaplan-Meier plot; 2-tailed, 2-stample t test of average number of stools per day; linear model of demographic data	
Population analysed	Intent-to-treat	Modified ITT as some subjects did not complete follow up. Details specified.
Missing data	Yes	10 participants had incomplete follow up. Considered to be accounted for in Kaplan-Meier plot.

Characteristics of included studies	DIARRHOEA		
Study ID	Jacobs 2006		
Study reference	Jacobs, J., Guthrie, B. L., Montes, G. A., Jacobs, L. E., Mickey-Colman, N., Wilson, A. R., & DiGiacomo, R. (2006). Homeopathic combination remedy in the treatment of acute childhood diarrhea in Honduras [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. Journal of Alternative & Complementary Medicine, 12(8), 723-732.		
Study design	RCT	Randomised by sequential assignment to previously coded vials (which were also randomised using a random-numbers table).	
Author affiliation	All seven authors were from a university in the USA		
Source of funds	Boiron Research Foundation (Newtown Square, Pennsylvania) and by Puget Sound Partners for Global Health's Research and Technology Project (Seattle, Washington)		
Declared interests of study authors	No information		
Setting / provider	Two municipal clinics in the Metropolitan Health District of Honduras		
Country(s) / region	Honduras		
Enrolment period	March 1 2004 to August 31 2004		
Length of intervention + follow up	Unclear for intervention. Follow up for up to 7 days. (Until symptoms resolved).		
Description of population	*N=*	*Description*	
participants	301	Acute childhood diarrhoea	
details	Inclusion criteria: Children between 5 mths and 6 years old presenting with acute diarrhoea (defined as the passage of three or more unformed stools during the previous 24 hours). Exclusion criteria: Children who had diarrhoea lasting more than 4 days, had visible blood in their stool, were severely dehydrated, lived outside the geographical area served by the clinics (to avoid difficulty with follow up home visits).		
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*
Intervention #1	Non-individualised	150	Non-individualised homeopathic combination medicine (Arsenicum album, Calcerea carbonica, Chamomilla, Podohyllum, and sulphur), given in 30c potency via sucrose/lactose pellets, with two tablets to be taken orally after each unformed stools.
Intervention #2			

Characteristics of included studies	DIARRHOEA					
Study ID	Jacobs 2006					
Comparator #1 (control)	Placebo	151	Administered as per intervention			
Comparator #2 (other)						
Comparator #3 (other)						
Co-interventions	Oral rehydration therapy according to WHO protocols.					
Is comparator clearly inactive?	Yes	Comparison=control				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptom duration	Up to 7 days	Duration of diarrhoea	Card provided to parents to record the type and time of each stool, examined and reviewed by nurse	Time from study entry until the first 2 consecutive days with <3 unformed stools
2	Primary	Symptom severity	Up to 7 days	Average daily rate of unformed stools during follow up	Card provided to parents to record the type and time of each stool, examined and reviewed by nurse	Calculated by dividing the total number of unformed stools by the number of days of follow up.
3	Primary	Symptom severity	Up to 7 days	Total number of unformed stools during follow up	Card provided to parents to record the type and time of each stool, examined and reviewed by nurse	
4	--	--				
5	--	--				
NOTE:	--	--				
Method of analysis						

Characteristics of included studies	DIARRHOEA	
Study ID	Jacobs 2006	
Statistics	Pearson's X2 test and two-sample t-test for baseline characteristics; Kaplan-Meir plot for survival profile; Cox Proportional Hazards model for the effect of treatment; Hazard ratios as the relative possibility of diarrhoea resolution; time-varying covariate model for effect of treatment group over time; linear regression model for the relationship between treatment and rate of unformed stools; Wilcoxon rank sum test of the effect of treatment on total number of unformed stools; univariate adjustment for precision during secondary analysis	
Population analysed	Intent-to-treat	Modified ITT as some subjects did not complete follow up. Details specified.
Missing data	Yes	27 participants had incomplete follow up. Considered to be accounted for in Kaplan-Meier plot.

Characteristics of included studies	DIARRHOEA		
Study ID	Patel 2010		
Study reference	Patel, M., et al. (2010). "An approach to acute diarrhoeal disorders through sector and constitutional homoeopathic treatment in tribal children attending balwadis." Indian journal of research in homoeopathy 4(4): 36-48.		
Study design	quasi-RCT		No information
Author affiliation	No information		
Source of funds	No information		
Declared interests of study authors	No information		
Setting / provider	Dr. M. L. Dhawale Memorial Trust's Community Health Centre Bhopoli, Taluka Vikramgarh, Dist. Thane		
Country(s) / region	India		
Enrolment period	November 2004 to December 2007		
Length of intervention + follow up	Intervention was discontinued once improvement had taken place plus single constitutional dose. Follow up for a minimum period of one year (up to 2 years).		
Description of population	*N=*	*Description*	
participants	342	Acute childhood diarrhoea	
details	Inclusion criteria: Children between age groups 1 to 7 years having recurrent episodes of diarrhoea, including children with moderate malnutrition. Exclusion criteria: Children having severe malnutrition.		
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include # treatment sessions, session duration, program duration, remedy chosen, potency and dosage).*
Intervention #1	Individualised	100	Individualised, acute, homeopathic remedy
Intervention #2	Individualised	100	Individualised, acute, homeopathic remedy followed by constitutional remedy (single dose follow resolve of

Characteristics of included studies	DIARRHOEA					
Study ID	Patel 2010					
Comparator #1 (control)	Placebo	100	Administered as per intervention			
Comparator #2 (other)						
Comparator #3 (other)						
Co-interventions	Ancillary therapy. 75% of cases oral rehydration therapy was used and in 25% of cases IV fluids were used.					
Is comparator clearly inactive?	Yes	Comparison=control				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Not specified	Aggravation	Minimum 1 year (up to 2 years)	Clinical grading of diarrhoea (Grade 1 to Grade 5)	Considered if the grade of diarrhoea was increased by at least one grade e.g. Grade 2 diarrhoea becoming to Grade 3	
2	Not specified	Amelioration	Minimum 1 year (up to 2 years)	Clinical grading of diarrhoea (Grade 1 to Grade 5)	Considered if grade of diarrhoea was decreased at least by two grades or absence of acute diarrhoea e.g. Grade 3 diarrhoea becoming Grade 1	
3	Not specified	Status quo	Minimum 1 year (up to 2 years)	Clinical grading of diarrhoea (Grade 1 to Grade 5)	If there was no change in grade of diarrhoea e.g. Grade 3 remaining Grade 3	
4	--	--				
5	--	--				
NOTE:	--	--				
Method of analysis						

Characteristics of included studies	DIARRHOEA	
Study ID	Patel 2010	
Statistics	Chi-Square test with Yates correction to assess differences in results	
Population analysed	Per protocol	42 cases were lost in follow up mainly due to high rate of migration out of the area. Total cases analysed were 300.
Missing data	Yes	42 cases were lost in follow up and their data not included in analyses.

Characteristics of included studies	Reflux		
Study ID	**Dossett 2015**		
Study reference	Dossett, M. L., Mu, L., Davis, R. B., Bell, I. R., Lembo, A. J., Kaptchuk, T. J., & Yeh, G. Y. (2015). Patient-provider interactions affect symptoms in gastroesophageal reflux disease: A pilot randomized, double-blind, placebo-controlled trial. PLoS ONE [Electronic Resource], 10(9) (no pagination).		
Study design	RCT	Subjects were randomised using permuted blocks randomisation with randomly varying block sizes of four or eight.	
Author affiliation	6 authors are affiliated with a medical centre in the United States, 3 authors are affiliated with a university in the United States, 1 author is affiliated with another university in the United States		
Source of funds	Medical centre in the United States		
Declared interests of study authors	Various authors consult for various pharmaceutical/health companies, however no products from any were involved in the study.		
Setting / provider	Beth Israel Deaconess Medical Center (BIDMC) clinical research centre		
Country(s) / region	Boston, United States		
Enrolment period	June 2013 and April 2014		
Length of intervention + follow up	1 wk for baseline measurement, 2 wks of treatment and follow up		
Description of population	*N=*	*Description*	
participants	24	Adults with gastroesophageal reflux disease (GERD)	
details	Inclusion criteria: age 18-80, fluent in written and spoken English, who endorsed heartburn symptoms 3 or more days per wk for the past mth, individual's actively taking proton pump inhibitors or H2 receptor blockers at stable doses for more than two wks but still had breakthrough symptoms Exclusion criteria: individuals with Chron's disease, systemic sclerosis, known active ulcer disease, gastric cancer, untreated/active Barrett's esophagitis, significant pain or difficulty with swallowing, heavy alcohol use (defined by >6 drinks/wk for women and >13 drinks/wk for men), concurrent pregnancy, dementia, or uncontrolled psychiatric disease, individuals who were unable to complete a paper symptom diary for at least 6 of 7 days, who had used homeopathy or had taken herbal products for GERD-related symptoms within the past two wks, or had taken greater than 12 doses of NSAIDS within the prior 30 days (aspirin < 325mg daily was allowed), subjects with lactose intolerance.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Non-individualised	6	Standard length interview (average 18 minutes) and Acidil - 2 tablets dissolved under the tongue 3 times per day approximately 15 minutes prior to meals

Characteristics of included studies	Reflux						
Study ID	**Dossett 2015**						
Intervention #2	Non-individualised	6	Expanded length interview (average 42 minutes) and Acidil - 2 tablets dissolved under the tongue 3 times per day approximately 15 minutes prior to meals				
Comparator #1 (control)	Placebo	6	Standard length interview (average 18 minutes) and placebo - 2 tablets dissolved under the tongue 3 times per day approximately 15 minutes prior to meals				
Comparator #1 (control)	Placebo	6	Expanded length interview (average 42 minutes) and placebo - 2 tablets dissolved under the tongue 3 times per day approximately 15 minutes prior to meals				
Comparator #3 (other)							
Co-interventions	Subject provided with rescue antacid that they were permitted to take for severe breakthrough symptoms.						
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis					
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*	
1	Primary	GERD symptoms	Change from baseline (2 wks)	Daily symptom diary, number of responders	number of participants with a 50% or greater improvement in GERD symptom severity from baseline to follow-up; higher is worse		
2	Primary	GERD symptoms	Change from baseline (2 wks)	Gastrointestinal Symptom Related Scale (GSRS reflux score)	number of participants with a 50% or greater improvement in GERD symptom severity from baseline to follow-up;		
3	Primary	HRQoL	Change from baseline (2 wks)	GERD-Health-Related Quality of Life Instrument (GERD-HRQL score)	number of participants with a 50% or greater improvement in GERD symptom severity from baseline to follow-up;		
4	Not specified	Dyspepsia symptoms	Change from baseline (2 wks)	Daily symptom diary, number of responders	number of participants with 50% or greater improvement in dyspepsia symptom severity from baseline to follow up		
Method of analysis							
Statistics	Exact logistic model, analysis of covariance (ANCOVA), Shapiro-Wilk text, Wilcoxon rank sum tests, chi square tests						
Population analysed	Intent-to-treat	Intent-to-treat analysis conducted.					
Missing data	No	No participants lost to follow up					

Characteristics of included studies	Dyspepsia		
Study ID	**Paterson 2003**		
Study reference	Paterson, C., Ewings, P., Brazier, J. E., & Britten, N. (2003). Treating dyspepsia with acupuncture and homeopathy: Reflections on a pilot study by researchers, practitioners and participants. Complementary Therapies in Medicine, 11(2), 78-84.		
Study design	RCT	Randomisation was in blocks of four, and serially numbered opaque envelopes were used to achieve concealed allocation. However, patients nominated preference of homeopathy and acupuncture and were then randomised.	
Author affiliation	1 author affiliated with a medical centre in the United Kingdom; 1 author affiliated with a hospital in the United Kingdom; 1 author affiliated with a research school in the United Kingdom; 1 author affiliated with an academic institute in the United Kingdom		
Source of funds	Combination of government and research funding		
Declared interests of study authors	No information		
Setting / provider	One general practice in the United Kingdom		
Country(s) / region	United Kingdom		
Enrolment period	8 mths in 1999		
Length of intervention + follow up	6 mth intervention + one follow up at 12 mths		
Description of population	*N=*	*Description*	
participants	60	People (>16 years) with dyspepsia	
details	Inclusion criteria: people (>16 years) with dyspepsia Exclusion criteria: those with symptoms of less than 2 wks, those under 16 years, pregnant, or unable to attend the surgery for treatment; those who required specialist referral for investigation or treatment of serious disease; those who had received complementary therapy for the presenting condition in the last 3 mths.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	21	Homeopathy (range from 0-8 treatments; mean 4 treatments)

Characteristics of included studies	Dyspepsia					
Study ID	**Paterson 2003**					
Intervention #2	--	--	--			
Comparator #1 (control)	Inactive control	19	Normal general practitioner care			
Comparator #1 (control)	Active control	20	Acupuncture (range from 4-18 treatments; mean 11 treatments)			
Comparator #3 (other)						
Co-interventions	Nil					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Inactive control	
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptom severity	Measured at 6 wks, 4 and 6 mths. 6 wk point is primary outcome	Measure Yourself Medical Outcome Profile (MYMOP)	Scores range from 0-6 Positive change is improvement	Patients nominate symptoms they would like to assess (something they need assistance with)
2	Primary	Psychological wellbeing	Measured at 6 wks, 4 and 6 mths. 6 wk point is primary outcome	General Wellbeing Index (GWBI)	Scores range from 22-110 Positive change is improvement	
3	Not specified	Quality of life	6 wks, 4 and 6 mths	SF-36 health survey	Scores range from 0-100 for each domain (8 domains) Higher score is better quality of life	
4	--	--	--	--	--	--
Method of analysis						
Statistics	Unpaired t-test of mean change; no other information provided					
Population analysed	Intent-to-treat	ITT conducted, however, results modified ITT analysis provided				
Missing data	Yes	<5% of missingness				

Characteristics of included studies	Infantile colic		
Study ID	**Raak 2019**		
Study reference	Raak, C., Krueger, P., Klement, P., De Jaegere, S., Weber, S., Keller, T., Ilyenko, L., Martin, D., & Ostermann, T. (2019). Effectiveness of a homeopathic complex medicine in infantile colic: A randomized multicenter study. Complementary Therapies in Medicine, 45, 136-141.		
Study design	RCT	Block randomisation with a block size of 4 was electronically generated and 50% of patients allocated to either intervention or placebo	
Author affiliation	2 authors are affiliated with an integrative medical institute in Germany; 1 author is affiliated with a research institute in Germany; 1 author is affiliated with a homeopathic union in Germany; 1 author is affiliated with a statistics consulting firm in Germany; 1 author is affiliated with a university in Russia; 1 author is associated with a university in Germany		
Source of funds	German homeopathic institute		
Declared interests of study authors	3 authors are employees of the university which was subsidised by the German homeopathic institute, 2 authors are employed by the statistics consulting firm that completed the statistical analysis for the study, 1 author received payment for the study, 2 authors are employees of the German homeopathic institute, and 1 author had nothing to declare		
Setting / provider	3 medical centres in Russia		
Country(s) / region	Russia		
Enrolment period	2009		
Length of intervention + follow up	10 days		
Description of population	*N=*	*Description*	
participants	125	Babies <6 mths who showed infantile colic symptoms or flatulence	
details	Inclusion criteria: children of both genders, <6 mths, who showed infantile colic symptoms or flatulence of any origin and for whom parents had signed an informed consent form before any study-specific procedure. Exclusion criteria: cases of intestinal infectious diseases, severe concomitant diseases (including severe renal, cardiac, hepatic, and/or immunosuppressive diseases), clinically significant thyroid dysfunction, cancer, known or suspected hypersensitivity to any components of the study medication, participation in another clinical study during the 6 mths prior to study enrolment, and in cases of any other drugs for infantile colic or flatulence within 30 days prior to study enrolment.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Non-individualised	74	Enterokind. 3 drops every hour, up to a maximum of 6 times every day. Upon improvement, as individually determined by the investigator, children received 3 drops, 3 times a day.

Characteristics of included studies	Infantile colic					
Study ID	**Raak 2019**					
Intervention #2	--	--	--			
Comparator #1 (control)	Active control	51	Simethicone. 1 teaspoon, 3-5 times per day.			
Comparator #1 (control)	--	--	--			
Comparator #3 (other)						
Co-interventions	None reported.					
Is comparator clearly inactive?	No	Comparison=other				
Outcomes (measure, description, measurement tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptom duration	Change from baseline (10 days)	Complaint Score (CS) Maximum score 17	9 complaints: sleep disturbances, unmotivated agitation, appetite disturbances, increased crying during and after feeding, regurgitation, vomiting (each 0, 1 or 2), constipation (0, 1, 2, or 3), loose stools and flatulence (each	
2	Primary	Symptom frequency	Change from baseline (10 days)	Objective Symptoms Score (OSS) Maximum score 22	15 objective symptoms: skin pallor, dry skin, mouth dryness, geographic tongue, abdominal bloating, borborgymus, pain on palpitation, intestinal spasms on	
3	Secondary	Complaint score	Change from baseline (10 days)	Change in individual complaint severity		
4	Secondary	Objective symptom score	Change from baseline (10 days)	Change in individual symptom severity		
Method of analysis						
Statistics	ANCOVA repeated measures modelling					
Population analysed	Intent-to-treat	Intent-to-treat analysis conducted.				
Missing data	Yes	<5% missingness (5 lost to follow up)				

Characteristics of included studies	IRRITABLE BOWEL SYNDROME		
Study ID	**Peckham 2012**		
Study reference	Peckham EJ, Relton C, Raw J, Walters C, Thomas K, Smith C. A protocol for a trial of homeopathic treatment for irritable bowel syndrome. BMC Complementary & Alternative Medicine. 2012;12:212. Peckham EJ, Relton C, Raw J, Walters C, Thomas K, Smith C, et al. Interim results of a randomised controlled trial ofhomeopathic treatment for irritable bowel syndrome. Homeopathy: the Journal of the Faculty of Homeopathy. 2014;103(3):172-7. ISRCTN90651143		
Study design	RCT	Shuffling of sealed, opaque envelopes containing the allocation	
Author affiliation	The authors are affiliated with several universities in the UK		
Source of funds	This study was funded by Barnsley Hospital Small Grants Fund, Friends of Barnsley Hospital and the Homeopathy Research Institute.		
Declared interests of study authors	The authors declared no conflict of interest		
Setting / provider	Community, participants recruited from primary or secondary care		
Country(s) / region	UK		
Enrolment period	February 2006 to September 2008		
Length of intervention + follow up	6 mth intervention period, 1 year follow up		
Description of population	*N=*	*Description*	
participants	94	Irritable bowel syndrome	
details	Inclusion criteria: aged 18 or over, IBS diagnosis using ROME III criteria, consent to complete and return questionnaires, Scored <=100, fluent in English Exclusion criteria: major gastrointestinal surgery within 6 mths,pregnant or breast feeding, current diagnosis of cancer, unstable psychiatric disorder, or other serious physical illness		
Description of intervention/ comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	16	Individualised homeopathy, homeopaths were able to prescribe any product in a potency and frequency of their choice, participants were offered 5x 1 hour sessions of homeopathic treatment over 6 mths
Intervention #2	--	--	--

Characteristics of included studies	IRRITABLE BOWEL SYNDROME					
Study ID	**Peckham 2012**					
Comparator #1 (control)	Inactive control	60	No intervention			
Comparator #2 (other)	Active control	18	Supportive listening, 5x 1 hour sessions over 6 mths. Supportive listening is based on the theories of Carl Rogers and involves active listening skills such as empathising, reflecting, summarising and paraphrasing. Sessions are delivered by trained psychotherapists.			
Comparator #3 (other)	--	--			--	
Co-interventions	Usual care					
Is comparator clearly inactive?	Yes	Comparison=control	No intervention			
Outcomes (meaure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptom Severity	Baseline, post intervention (26 wks)	IBS Symptom Severity Score	Higher score is worse, scores range from 75-500 50 points is considered clinically relevant change	
2	Secondary	Anxiety	Baseline, post intervention (26 wks)	Hospital Anxiety and Depression Scale - Anxiety	Higher score is worse, scores range from 0-21	
3	Secondary	Depression	Baseline, post intervention (26 wks)	Hospital Anxiety and Depression Scale - Depression	Higher score is worse, scores range from 0-22	
4	Secondary	Health related quality of life	Baseline, post intervention (26 wks)	EQ-5D	Higher score is better	
Method of analysis						
Statistics	Independent t test to compare groups					
Population analysed	Intent-to-treat	ITT basis specified in trial protocol, modified ITT conducted as participants who did not return the questionnaire were not included in the analysis.				
Missing data	Yes	12/94 (12.8%) of participants did not return the follow up questionnaire. No adjustment for missing data was presented.				

Characteristics of included studies	PSORIASIS		
Study ID	**Bernstein 2006**		
Study reference	Bernstein, S., et al. (2006). "Treatment of mild to moderate psoriasis with Relieva, a Mahonia aquifolium extract--a double-blind, placebo-controlled study." American Journal of Therapeutics 13(2): 121-126.		
Study design	quasi RCT	Participants randomised to placebo or control. Process of randomisation not specified.	
Author affiliation	Not detailed. Possibly Dermatology and Cosmetic Center in New York.		
Source of funds	Not detailed, but specified in part by Apollo Pharmaceuticals Inc.		
Declared interests of study authors	Not specified		
Setting / provider	6 sites in the United States and Canada		
Country(s) / region	United States and Canada		
Enrolment period	August 2004 to February 2005		
Length of intervention + follow up	Total 12 wks, with follow up at 4, 8, and 12 wks.		
Description of population	*N=*	*Description*	
participants	200	Patients with mild to moderate psoriasis	
details	Inclusion criteria: patients between the ages of 18 to 80 years, in overall good health, with current mild to moderate psoriasis covering less than 10-15% of the body. Exclusion criteria: painful or inflamed lesions, inter-regionous psoriasis, extremely hypertrophic lesions, and severe psoriasis. Patients using topical psoriasis medications within the past 2 wks, and those taking systemic (oral, intravenous, intramuscular, or intradermal) medications for psoriasis in the past 28 days, those using steroids, immunosuppressive medications, and cyclooxygenase-2 anti-inflammatory drugs, and those using any medication conflicting with the product ingredients. Women planning to become pregnant within 90 days of the start of the study and pregnancy or lactating women or women not taking medically approved birth control.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Non-individualised	97	Topical Relieva (mahonia aquifolium) applied twice a day to the selected area (the selected area was a 4x4cm area of the skin selected by the investigator using a precut template)
Intervention #2			
Comparator #1 (control)	Placebo	74	Administered as per intervention.
Comparator #2 (other)			

Characteristics of included studies	PSORIASIS					
Study ID	**Bernstein 2006**					
Comparator #3 (other)						
Co-interventions	None specified					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Disease severity	Initial visit (wk 0) and wk 12	Psoriasis Area Severity Index (PASI)	Conducted by the physician	Higher score indicates more active disease
2	Secondary	Quality of life	At each visit (wk 0, 4, 8, and 12)	Quality of Life Index (QLI) Questionnaire	Completed by patient	Higher score indicates greater impact on quality of life
3	--	--	--	--	--	--
4						
5						
add rows as needed						
Method of analysis						
Statistics	Mean and standard deviations (SD), median, and minimum and maximum changes (min and max) were reported for continuous variables. Frequencies and percentages were reported for categorical variables. Independent sample t tests were used to compare differences between groups for continuous variables, and Fisher exact tests were used to test between group differences for categorical variables.					
Population analysed	Intent-to-treat	Intent-to-treat analysis.				
Missing data	Yes	Discontinuation due to no response, adverse events, relocation, noncompliance, and death (non-treatment related).				

Characteristics of included studies	PSORIASIS		
Study ID	**Wiesenauer 1992**		
Study reference	Wiesenauer, M. (1992). "Research in homoeopathy: efficacy and tolerance of Mahonia aquifolium during treatment of psoriasis vulgaris." Extracta Dermatologica 16/12: 23-31.		
Study design	quasi RCT	Participants legs randomised to either homeopathy or placebo. Process of randomisation not specified.	
Author affiliation	Each author affiliated with a different university in Germany.		
Source of funds	One author received funding from a private source from Germany.		
Declared interests of study authors	Not specified		
Setting / provider	Surgeries of family physicians and dermatologists.		
Country(s) / region	Germany		
Enrolment period	Autumn 1990 to spring 1992		
Length of intervention + follow up	Total therapy length was individually assigned by the treating physician. The trial coordinators suggested a length of eight wks		
Description of population	*N=*	*Description*	
participants	82	Patients with clinically diagnosed psoriasis vulgaris of all degrees of severity	
details	*Inclusion criteria:* clinically verified psoriasis vulgaris, age > 16 years, symmetrical manifestation in both body sides (i.e. test and contralateral control area), no actual application of systemic remedies potentially influencing the course of disease (e.g. corticoids), expected compliance based on the physicians judgement, no application of local dermatological therapies, no inclusion in any other clinical trial, informed consent. *Exclusion criteria:* not specified		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Non-individualised	82	Topical (Mahonia aquifolium ointment) massaged into afflicted areas two to three times a day and bandages smeared with the ointments are night.
Intervention #2			
Comparator #1 (control)	Placebo	82	Administered as per intervention.
Comparator #2 (other)			

Characteristics of included studies	PSORIASIS					
Study ID	**Wiesenauer 1992**					
Comparator #3 (other)						
Co-interventions	None specified					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Disease severity	Individually assigned (median treatment period was 4 wks)	Symptoms unchanged	Self-assessment by patient and treating physician	
2	Primary	Disease severity	Individually assigned (median treatment period was 4 wks)	Symptoms improved	Self-assessment by patient and treating physician	
3	Primary	Disease severity	Individually assigned (median treatment period was 4 wks)	Symptoms disappeared completely	Self-assessment by patient and treating physician	
4						
5						
add rows as needed						
Method of analysis						
Statistics	Marginal Homogeneity Test in 3x3 contingency tables; Bonferroni-Holm-Procedure; multiple logistic regression; Wald's two-sided asymptotic test					
Population analysed	Intent-to-treat	Modified intent-to-treat due to violated protocols and missing data.				
Missing data	Yes	2 participants not included in final outcome analysis. Not specific which treatment group.				

Characteristics of included studies	Rheumatoid arthritis		
Study ID	**Brien 2004**		
Study reference	Brien S, Lachance L, Lewith GT. Are the therapeutic effects of homeopathy attributed to the consultation, the homeopathic remedy, or both? A protocol for a future exploratory feasibility trial in patients with rheumatoid arthritis. J Altern Complement Med. 2004;10(3):499-502. Brien S, Lachance L, Prescott P, McDermott C, Lewith G. Homeopathy has clinical benefits in rheumatoid arthritis patients that are attributable to the consultation process but not the homeopathic remedy: a randomized controlled clinical trial. Rheumatology (Oxford, England). 2011;50(6):1070-82. Brien SB, Leydon GM, Lewith G. Homeopathy enables rheumatoid arthritis patients to cope with their chronic ill health: a qualitative study of patient's perceptions of the homeopathic consultation. Patient Educ Couns. 2012;89(3):507-16.		
Study design	RCT	Computer generated random numbers. Allocation concealment using sealed envelopes	
Author affiliation	The authors were affiliated with universities in Southampton, UK and Michigan, US.		
Source of funds	This work was supported by the National Institute of Health Research (PDA04/CAMs2/02 to S.B. and project funding), the Samueli Institute, USA (for project funding), the Southampton Complementary Medicine Research Trust (for project funding) the Rufford Maurice Laing Foundation (to G.L.), Dreluso Pharmazeutika GmBH (complex homeopathic medication); and National Health Service Fund for Science (Poole R+D Hospital Trust; for study nurse and blood tests).		
Declared interests of study authors	The authors declared no conflict of interest		
Setting / provider	Multi-centre, participants recruited from outpatient rheumatology clinics		
Country(s) / region	UK		
Enrolment period	January 2006 - July 2008		
Length of intervention & follow up	24 wk treatment, 40 wk total follow up		
Description of population	*N=*	*Description*	
participants	83	Rheumatoid arthritis	
details	Inclusion criteria: aged >18 years, diagnosis of RA for >2 years, current disease activity: minimum DAS-28 score >2.6, patient global assessment >=30mm, stable medication >3 mths Exclusion criteria: severe RA (functional class IV), treatment with bDMARDs, severe comorbidities, used homeopathy for <3 mths, pregnant or breastfeeding, participated in an investigational trial within 45 days of enrolment		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Rheumatoid arthritis					
Study ID	**Brien 2004**					
Intervention #1	17	Individualised	Consultation + individualised homeopathy. Participants received homeopathic consultation from visit 2-6 (every 4 wks), initial consultation was 1hr, follow-up was 30 mins. Homeopath determined individual homeopathic product.			
Intervention #2	15	Non-individualised	Consultation + non-individualised homeopathy. Participants received homeopathic consultation from visit 2-6 (every 4 wks), initial consultation was 1hr, follow-up was 30 mins. Participants were posted homeopathic complex (Rheumaselect), taken 20 drops per dose 2x daily.			
Comparator #1 (control)	17	Placebo	Consultation + placebo. Participants received homeopathic consultation from visit 2-6 (every 4 wks), initial consultation was 1hr, follow-up was 30 mins. Participants were posted identical placebo.			
Comparator #2 (other)	18	Placebo	No consultation + placebo. Participants did not receive homeopathic consultation. Participants were posted placebo identical to the homeopathic complex product.			
Comparator #3 (other)	16	Active control	No consultation + non-individualised homeopathy. Participants did not receive homeopathic consultation. Participants were posted homeopathic complex (Rheumaselect), taken 20 drops per dose 2x daily.			
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo group	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*Other*
1	Primary	Overall disease impact	Baseline, every 4 wks	ACR20		
2	Primary	Health related quality of life	Baseline, every 4 wks	VAS (0-100mm)	Participant's general assessment of health. MCID is 35% change from baseline	
3	Secondary	Disease severity	Baseline, every 4 wks	DAS-28		
4	Secondary	Disease severity	Baseline, every 4 wks	ACR20 individual measures		
5	Secondary	Health related quality of life	Baseline, every 4 wks	Measure Yourself Medical Outcome Profile		

Characteristics of included studies	Rheumatoid arthritis				
Study ID	**Brien 2004**				
6	Secondary	Emotional function	Baseline, every 4 wks	Positive and Negative Affect Scale	
7	Secondary	Pain	Baseline, every 4 wks	VAS (0-100mm)	
8	Secondary	Safety	Baseline, every 4 wks	Adverse events	
9	Secondary	Functional disability	Baseline, every 4 wks	Health Assessment Questionnaire	Range 1-3
10	Secondary	Disease biomarkers	Baseline, every 4 wks	ESR, CRP	
Method of analysis					
Statistics	ITT using two-sided 5% confidence intervals. Randomisation was broken by statistician after data entry was completed. Logistic regression analysis assessed dichotomous data and analysis of co-variance assessed continuous data comparing changes from baseline to end of treatment. Mean (SD) and 95% CI are provided.				
Population analysed	Intent-to-treat	ITT analysis specified. Data on patients who withdrew were included in the analysis to the point of withdrawal.			
Missing data	Yes	27/83 participants did not complete treatment. Reasons for non-completion include adverse events, breaching inclusion criteria, non-compliance, and participant not wishing to continue.			

Characteristics of included studies	Rheumatoid arthritis		
Study ID	**Fisher 2001**		
Study reference	Fisher P, Scott DL. A randomized controlled trial of homeopathy in rheumatoid arthritis. Rheumatology. 2001;40(9):1052-5.		
Study design	quasi RCT	No mention of randomisation sequence	
Author affiliation	The authors were affiliated with a homeopathic hospital and university hospital in the UK		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Participants recruited from a single rheumatology clinic		
Country(s) / region	UK		
Enrolment period	1986-1994		
Length of intervention & follow up	3 mth intervention followed by 3 mth crossover		
Description of population	*N=*	*Description*	
participants	112	Definite of classical rheumatoid arthritis	
details	Inclusion criteria: definite or classical rheumatoid arthritis, seropositive for rheumatoid factor, receiving stable doses of single non-steroidal anti-inflammatory drugs or >=3 mths of single disease-modifying anti-rheumatic drugs with or without NSAIDs for >=6 mths Exclusion criteria: severely disabled (functional class IV), taken systemic steroids in the previous 6 mths, withdrawn from DMARD therapy in previous 12 mths		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Rheumatoid arthritis					
Study ID	**Fisher 2001**					
Intervention #1	NR	Individualised	Participants received a consultation with a homeopath, where a homeopathic product was prescribed. A list of 42 products were available, only one product was prescribed at each visit. For products in the 6cH dilution, participants were instructed to suck one pilule twice daily. For products in the 30cH dilution, participants were instructed to suck two pilules in the morning twice wkly.			
Intervention #2	--	--	--			
Comparator #1 (control)	NR	Placebo	Participants also received consultation with homeopath but were dispensed placebo instead of active treatment.			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	DMARDs or NSAIDs					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*Other*
1	Primary	Pain	Baseline, 3 mths, 6 mths	VAS (0-100mm)	Higher is worse	
2	Primary	Tenderness	Baseline, 3 mths, 6 mths	Ritchie articular index		
3	Primary	Stiffness	Baseline, 3 mths, 6 mths	Duration of morning stiffness	Higher is worse	
4	Primary	Disease biomarkers	Baseline, 3 mths, 6 mths	Erythrocyte sedimentation rate (ESR)		
5	--	--				

Characteristics of included studies	Rheumatoid arthritis	
Study ID	**Fisher 2001**	
6	--	--
7	--	--
8	--	--
9	--	--
10	--	--
Method of analysis		
Statistics	Data were evaluated independent using non-parametric statistical tests by a rheumatologist before randomisation code was broken	
Population analysed	Per protocol	Not specified but interpreted per protocol. Participants who did not attend two consecutive appointments were withdrawn and replaced.
Missing data	Yes	58/112 participants completed the trial. Reasons for drop out include changing conventional medication, intercurrent illness or surgery, failure to attend appointments, withdrawn consent.

Characteristics of included studies	Periarthritis (shoulder)		
Study ID	**Khitrov 2009**		
Study reference	Khitrov NA. The use of artrofoon in the therapy of disorders of the paraarticular apparatus. Bull Exp Biol Med. 2009;148(3):478-81.		
Study design	quasi RCT	Quasi-randomised	No details provided regarding randomisation or allocation concealment
Author affiliation	The author was affiliated with a medical research centre in Russia		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Not reported		
Country(s) / region	Russia		
Enrolment period	Not reported		
Length of intervention & follow up	3 mth intervention, follow up not reported		
Description of population	*N=*	*Description*	
participants	60	People with periarthritis of the shoulder joint	
details	Not reported		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Periarthritis (shoulder)					
Study ID	**Khitrov 2009**					
Intervention #1	30	Non-individualised	Non-individualised homeopathy with Artrofoon (ultra low TNF-a). Treatment was given in 8 tablets per day for 3 mths; after attaining improvement, dose was lowered to 4 tablets per day.			
Intervention #2	--	--	--			
Comparator #1 (control)	30	Active control	Non-steroidal anti-inflammatory (NSAID), primarily diclofenac.			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	None reported					
Is comparator clearly inactive?	No	Comparison=other			NSAID	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*Other*
1	Not specified	Pain at rest	Baseline, 2 wks, 1 mth, 3 mths	VAS (0-100mm)	higher is worse	
2	Not specified	Pain during movement	Baseline, 2 wks, 1 mth, 3 mths	VAS (0-100mm)	higher is worse	
3	Not specified	Range of movement	Baseline, end of treatment (3 mths	Amplitude of should joint movement		
4	Not specified	Biochemical markers	Baseline, end of treatment (3 mths	Glucose		
5	Not specified	Biochemical markers	Baseline, end of treatment (3 mths	Total protein		

Characteristics of included studies	Periarthritis (shoulder)				
Study ID	**Khitrov 2009**				
6	Not specified	Biochemical markers	Baseline, end of treatment (3 mths	Transaminase	
7	Not specified	Biochemical markers	Baseline, end of treatment (3 mths	Bilirubin	
8	Not specified	Biochemical markers	Baseline, end of treatment (3 mths	Creatinine	
9	Not specified	Biochemical markers	Baseline, end of treatment (3 mths	Urea	
10	Not specified	Quality of life	Baseline, end of treatment (3 mths	Patient reported	Patient reported 'general state'
Method of analysis	--	--			
Statistics	Not reported				
Population analysed	Other (provide details)	*Not reported*			
Missing data	Not specified	*The number of participants randomised and analysed is not reported*			

Characteristics of included studies	Osteoarthritis (knee)		
Study ID	**Koley 2015**		
Study reference	Koley M, Saha S, Ghosh S. A double-blind randomized placebo-controlled feasibility study evaluating individualized homeopathy in managing pain of knee osteoarthritis. J Evid Based Complementary Altern Med. 2015;20(3):186-91. CTRI/2014/05/004589		
Study design	RCT	Computer generated random numbers. Confidentiality maintained by the statistician who did not influence the study.	
Author affiliation	The authors were affiliated with a research institute and hospital in India		
Source of funds	The authors received no financial support for the research		
Declared interests of study authors	The authors declared no conflict of interest		
Setting / provider	Participants recruited from an outpatient clinic		
Country(s) / region	India		
Enrolment period	January - October 2014		
Length of intervention & follow up	2 wk intervention, no follow up reported		
Description of population	*N=*	*Description*	
participants	60	Osteoarthritis (knee)	
details	Inclusion criteria: age 50-86, clinically diagnosed knee osteoarthritis, suffering from self-reported acute painful episodes, with or without involvement of other joints, already undergoing regular oral or topical analgesics or non-steroidal anti-inflammatory drug therapy, conventional drug therapies for comorbidities under control Exclusion criteria: severe degeneration of knee joint with marked joint narrowing, varus or valgus deformity of knee, non-ambulant patients, self-reported joint disorders other than OA, intra-articular injections within 2 wks, uncontrolled, unevaluated or complicated comorbidities including diabetes or hypertension, vital organ failure, significant knee surgery within 6 mths, knee transplant, history of homeopathic treatment within 6 mths, self-reported immune compromised status, alcohol and/or drug dependence		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Osteoarthritis (knee)					
Study ID	**Koley 2015**					
Intervention #1	30	Individualised	Following recruitment and screening, a single individualised medicine was chosen based on the presenting symptoms, repertorisation and consultation with materia medica			
Intervention #2	--	--	--			
Comparator #1 (control)	30	Placebo	The control group were dispensed placebo by the pharmacist			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo group	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*Other*
1	Primary	Pain	Baseline, 1 wk, 2 wks	VAS (0-100mm)	higher is worse	
2	Primary	Stiffness	Baseline, 1 wk, 2 wks	VAS (0-100mm)	higher is worse	
3	Primary	Physical function	Baseline, 1 wk, 2 wks	VAS (0-100mm)	higher is worse	
4	Secondary	Pain	Baseline, 2 wks	Osteoarthritis Research Society International osteoarthritis intermittent/constant pain measure	Higher score is worse, scores standardised to 0-100	11 items (5 constant, 6 intermittent)
5	Secondary	Safety		Adverse events		

Characteristics of included studies	Osteoarthritis (knee)	
Study ID	**Koley 2015**	
6	--	--
7	--	--
8	--	--
9	--	--
10	--	--
Method of analysis		
Statistics	Outcomes at each time point were compared with paired *t* test, followed by post-hoc repeated measures analysis of variance. Bonferroni-Holm correction was made to set the significance at p<0.01, 2-tailed. Group differences were tested with independent *t* test, keeping significance at p<0.05, 2-tailed.	
Population analysed	Intent-to-treat	ITT analysis using last observation carried forward for missing data
Missing data	Yes	6/60 (10%) of participants dropped out. Reasons for drop out included deterioration (5) and loss to follow up (1).

Characteristics of included studies	Osteoarthritis (knee)		
Study ID	**Shealy 1998**		
Study reference	Shealy CN, Thomlinson RP, Cox RH, Borgmeyer V. Alternative medicine. Osteoarthritic pain: a comparison of homeopathy and acetaminophen. American Journal of Pain Management. 1998;8(3):89-91.		
Study design	quasi RCT	Method of randomisation not specified. The authors do not report on allocation concealment, however it is noted that staff did not know which intervention group participants were assigned.	
Author affiliation	The authors were affiliated with research institutes in the United States		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Not reported, likely community setting		
Country(s) / region	United States		
Enrolment period	Not reported		
Length of intervention & follow up	30 day follow up		
Description of population	*N=*	*Description*	
participants	65	Osteoarthritis (knee)	
details	Inclusion criteria: pre-existing diagnosis of osteoarthritis, at least moderate to severe pain on a daily basis for at least 6 mths Exclusion criteria: infectious arthritis, rheumatoid arthritis, neuropathy, corticosteroid treatment within 6 mths, significant renal or hepatic dysfunction		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Osteoarthritis (knee)					
Study ID	**Shealy 1998**					
Intervention #1	43	Non-individualised	Participants were asked to take 10 drops of a solution sublingually 4x daily for 1 mth. The homeopathic preparation consisted of Rhus Toxicodendron 12X, Causticum 12X and Lac Vaccinum 30X in a liquid base.			
Intervention #2	--	--	--			
Comparator #1 (control)	22	Active control	Acetaminophen 2600 mg daily.			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Both groups received placebo of the alternate treatment (i.e. homeopathy + placebo acetaminophen or acetaminophen + placebo homeopathy).					
Is comparator clearly inactive?	No	Comparison=other			Acetaminophen	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*Other*
1	Primary	Pain	Baseline, end of treatment (30 days)	VAS (0-100mm)	higher is worse	Daily pain diary
2	--	--				
3	--	--				
4	--	--				
5	--	--				

Characteristics of included studies	Osteoarthritis (knee)	
Study ID	**Shealy 1998**	
6	--	--
7	--	--
8	--	--
9	--	--
10	--	--
Method of analysis		
Statistics	A two-way mixed ANOVA test was performed with one between group factor (treatment arm) and one within group factor (baseline vs post treatment).	
Population analysed	Other (provide details)	*Not reported*
Missing data	Not specified	The number of participants randomised and analysed is not reported

Characteristics of included studies	Osteoarthritis (hip and knee)		
Study ID	**Shipley 1983**		
Study reference	Shipley M, Berry H, Broster G, Jenkins M, Clover A, Williams I. Controlled trial of homoeopathic treatment of osteoarthritis. Lancet. 1983;1(8316):97-8.		
Study design	quasi RCT	crossover trial	Method of randomisation not specified. The authors do not report on allocation concealment.
Author affiliation	The authors were affiliated with various hospitals in the UK		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Not reported, likely community setting		
Country(s) / region	UK		
Enrolment period	Not reported		
Length of intervention & follow up	2 wks of each treatment, 6 wks total		
Description of population	*N=*	*Description*	
participants	36	Osteoarthritis (hip or knee)	
details	*Inclusion criteria:* satisfied clinical and radiological criteria for osteoarthritis of one or more hips or knees *Exclusion criteria:* defined by Helsinki Convention, previously received *Rhus tox.* or fenoprofen		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Osteoarthritis (hip and knee)					
Study ID	**Shipley 1983**					
Intervention #1	NR	Individualised	Rhus tox. 6X, 5 drops, 3x daily within half an hour of food			
Intervention #2	--	--	--			
Comparator #1 (control)	NR	Placebo	Placebo 3x daily after meals			
Comparator #2 (other)	NR	Active control	Fenoprofen: 2 capsules containing 300 mg, 3x daily after meals			
Comparator #3 (other)	--	--	--			
Co-interventions	Paracetamol					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo group	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*Other*
1	--	Pain at rest	Baseline, end of treatment (2 wks)	VAS (0-10 cm)	higher is worse	
2	--	Pain during movement	Baseline, end of treatment (2 wks)	VAS (0-10 cm)	higher is worse	
3	--	Pain at night	Baseline, end of treatment (2 wks)	VAS (0-10 cm)	higher is worse	
4	--	Pain	Baseline, end of treatment (2 wks)	4-point pain score		
5	--	Medication use	End of treatment (2 wks)	Paracetamol return count	Higher score is better	

Characteristics of included studies	Osteoarthritis (hip and knee)	
Study ID	**Shipley 1983**	
6	--	--
7	--	--
8	--	--
9	--	--
10	--	--
Method of analysis		
Statistics	Not reported	
Population analysed	Other (provide details)	Not reported
Missing data	Yes	3/36 participants did not complete the study due to aggravation of symptoms (2) or total hip replacement (1).

Characteristics of included studies	Osteoarthritis (knee)		
Study ID	**Strosser 2000**		
Study reference	Strosser W, Weiser M. Patients with gonarthrosis gaining back mobility - Homoeopathic in a double-blind comparison. Biologische medizin. 2000;29(6):295-9.		
Study design	quasi RCT	Method of randomisation not specified. The authors do not report on allocation concealment.	
Author affiliation	Not reported		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Multi-setting, 13 orthopaedic practices		
Country(s) / region	Germany		
Enrolment period	Not reported		
Length of intervention & follow up	10 wk intervention, no further follow up reported		
Description of population	*N=*	*Description*	
participants	121	Gonarthrosis (knee)	
details	Inclusion criteria: slight or medium-severe gonarthrosis for at least 6 mths Exclusion criteria: not reported		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Osteoarthritis (knee)					
Study ID	**Strosser 2000**					
Intervention #1	60	Non-individualised	Zeel comp. 3x per day for 10 wks			
Intervention #2	--	--	--			
Comparator #1 (control)	61	Active control	Diclofenac 3x per day for 10 wks			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Both groups received placebo of the alternate treatment (i.e. homeopathy + placebo diclofenac or diclofenac + placebo homeopathy).					
Is comparator clearly inactive?	No	Comparison=other			Diclofenac	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*Other*
1	Primary	Disease severity	Baseline, 2, 4, 6, 10 wks	WOMAC	Higher score is worse, scores range 0-96	
2	--	--				
3	--	--				
4	--	--				
5	--	--				

Characteristics of included studies	Osteoarthritis (knee)	
Study ID	**Strosser 2000**	
6	--	--
7	--	--
8	--	--
9	--	--
10	--	--
Method of analysis		
Statistics	Not reported	
Population analysed	Other (provide details)	Not reported
Missing data	Not specified	The number of participants randomised and analysed is not reported

Characteristics of included studies	Osteoarthritis (knee)		
Study ID	**vanHaselen 2000**		
Study reference	van Haselen RA, Fisher PA. A randomized controlled trial comparing topical piroxicam gel with a homeopathic gel in osteoarthritis of the knee. Rheumatology (Oxford, England). 2000;39(7):714-9.		
Study design	RCT	Computer generated randomisation. Unclear allocation concealment.	
Author affiliation	The authors were affiliated with a homeopathic hospital in the UK		
Source of funds	The study was supported by a research grant from the Medical Scientific Department of VSM Geneesmiddelen, The Netherlands		
Declared interests of study authors	Not reported		
Setting / provider	Outpatients at a hospital rheumatology clinic		
Country(s) / region	UK		
Enrolment period	Not reported		
Length of intervention & follow up	4 wk intervention, no follow up		
Description of population	*N=*	*Description*	
participants	184	Osteoarthritis (knee)	
details	Inclusion criteria: radiographically confirmed osteoarthritis of the knee, moderate pain on movement, 18-86 years old, if oral NSAIDs or analgesics are taken, stable treatment during previous mth Exclusion criteria: oral piroxicam 7 days prior to or at any time during trial, previous use of piroxicam gel, additional joint disease other than OA, skin affections on the treated knee, known hypersensitivity to NSAIDs or Rhus toxicodendron, severe OA requiring surgical intervention, non-ambulant patients		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Osteoarthritis (knee)					
Study ID	**vanHaselen 2000**					
Intervention #1	89	Non-individualised	SRL gel (*Symphytum officinale, Rhus toxicodendron, Ledum palustre*). Participants were instructed to apply approximately 1g of gel, 3x daily. If both knees had OA, only the most clinically evident OA was treated.			
Intervention #2	--	--	--			
Comparator #1 (control)	91	Active control	Piroxicam gel (Feldene®) 0.5% piroxicam. Participants were instructed to apply approximately 1g of gel, 3x daily. If both knees had OA, only the most clinically evident OA was treated.			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	Paracetamol up to 3g per day allowed as rescue medication.					
Is comparator clearly inactive?	No	Comparison=other			Piroxicam	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*Other*
1	Primary	Pain on walking	Baseline, end of treatment (4 wks)	VAS (0-100mm)	higher is worse	5mm is MCID
2	Primary	Pain on palpitation	Baseline, end of treatment (4 wks)	4-point Likert	0=no pain, 1=pain without wincing, 2=pain with wincing, 3=pain leading to withdrawal	
3	Secondary	Medication use	Baseline, end of treatment (4 wks)	Paracetamol tablets used	Higher score is worse	
4	Secondary	Overall assessment	Baseline, end of treatment (4 wks)	Investigator assessed		
5	Secondary	Overall assessment	Baseline, end of treatment (4 wks)	Participant assessed		

Characteristics of included studies	Osteoarthritis (knee)				
Study ID	**vanHaselen 2000**				
6	Secondary	Relief during preceding wk	Baseline, end of treatment (4 wks)	VAS (0-100mm)	higher is worse
7	--	--			
8	--	--			
9	--	--			
10	--	--			
Method of analysis					
Statistics	Adjustment for covariates with pain reduction as dependent variable was achieved by analysis of covariance after the validity of the model had been verified. Change in Ritchie score and the overall assessment were analysed using the Exact Mann-Whitney U-test.				
Population analysed	Intent-to-treat	ITT population specified			
Missing data	Yes	12/184 participants did not have follow up outcome data available.			

Characteristics of included studies	Osteoarthritis (hand)		
Study ID	**Widrig 2007**		
Study reference	Widrig R, Suter A, Saller R, Melzer J. Choosing between NSAID and arnica for topical treatment of hand osteoarthritis in a randomised, double-blind study. Rheumatol Int. 2007;27(6):585-91.		
Study design	RCT	Prospective cohort	Computer generated random numbers in blocks of 4. Allocation concealment not reported
Author affiliation	The authors were affiliated with a rheumatology clinic and hospital in Switzerland		
Source of funds	Not reported		
Declared interests of study authors	Not reported		
Setting / provider	Multi-setting, community patients enrolled from 20 clinicals (12 GP, 6 rheumatology, 2 general medicine)		
Country(s) / region	Switzerland		
Enrolment period	May 2003 - March 2004		
Length of intervention & follow up	3 wk intervention, no follow up reported		
Description of population	*N=*	*Description*	
participants	204	Osteoarthritis (hand)	
details	Inclusion criteria: 18-88 years old, osteoarthritis diagnosis according to ARC criteria, pain intensity on the VAS of at least 40mm in the finger join, radiological confirmation of osteoarthritis in >=2 joints with radiographs <3 mths old and >=1 painful joint confirmed radiologically, discontinuation of all NSAIDs >10 days prior to study entry, discontinuation of all analgesics >3 days prior to study entry Exclusion criteria: secondary OA, trauma to the hand or arm within 2 mths, pain and stiffness due to tissue scarring, residual pain following fracture, dislocation or operation, tendinitis, carpal tunnel or other nerve compression syndrome, serious conditions (cancer, uncontrolled hypertension or heart failure), systematic of intra-articular corticosteroids, damaged skin, allergy to Asteraceae, intolerance to paracetamol		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Osteoarthritis (hand)						
Study ID	**Widrig 2007**						
Intervention #1	105	Individualised	Arnica gel. 4cm strip of gel to be gently rubbed over the affected joints 3x daily for 3 wks. Participants were instructed not to wash their hands for 1 hour after application.				
Intervention #2	--	--	--				
Comparator #1 (control)	99	Active control	Ibuprofen gel. 4cm strip of gel to be gently rubbed over the affected joints 3x daily for 3 wks. Participants were instructed not to wash their hands for 1 hour after application.				
Comparator #2 (other)	--	--	--				
Comparator #3 (other)	--	--	--				
Co-interventions	Paracetamol permitted as rescue medication. Long-term low-dose aspirin for cardiovascular disease was allowed at a maximum of 325 mg daily.						
Is comparator clearly inactive?	No	Comparison=other				Ibuprofen	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*Other*	
1	Primary	Pain	Baseline, end of treatment (3 wks)	VAS (0-100mm)	higher is worse	Most intense in previous 24h, worst affected finger	
2	Primary	Functional capacity	Baseline, end of treatment (3 wks)	Hand Algofunctional Index	Higher score is worse	10 questions, each rated 0-3	
3	Secondary	Pain	Baseline, end of treatment (3 wks)	Number of painful joints	Higher score is worse		
4	Secondary	Stiffness	Baseline, end of treatment (3 wks)	Intensity of morning stiffness	Higher score is worse		
5	Secondary	Stiffness	Baseline, end of treatment (3 wks)	Duration of morning stiffness	Higher score is worse		

Characteristics of included studies	Osteoarthritis (hand)				
Study ID	**Widrig 2007**				
6	Secondary	Medication use	Baseline, end of treatment (3 wks)	Analgesic consumption	Higher score is worse
7	Secondary	Overall assessment of efficacy	Baseline, end of treatment (3 wks)	Investigator assessed	
8	Secondary	Overall assessment of efficacy	Baseline, end of treatment (3 wks)	Participant assessed	
9	--	--			
10	--	--			
Method of analysis					
Statistics	Non-inferiority was set as the difference being not greater than 12% in each of the primary outcome measures (12mm in VAS, 3.6 points in HAI). Non-inferiority was considered to be shown in the left margin of the one-sided a-confidence limit of the Mann-Whitney statistic was greater than 0.322. Sample size calculated based on the assumption that the difference between the two groups would not be greater than 1 point on the HAI.				
Population analysed	Intent-to-treat	ITT analysis including all participants who were randomised and had a post-baseline value for comparison. Per protocol analyses also conducted.			
Missing data	Yes	Data missing for 6/204 participants			

Characteristics of included studies	Neck pain		
Study ID	**Gupta 2020**		
Study reference	Ctri. Effect of Predefined Homoeopathic Medicines in Cervical Spondylosis Pain Management. https://trialsearchwhoint/Trial2aspx?TrialID=CTRI/2011/12/002270. 2011. CTRI/2011/12/002270		
Study design	RCT	Computer generated random numbers. The investigator and pharmacist held the randomisation chart	
Author affiliation	Authors were affiliated with research institutes for homeopathy and clinical research institutes in India		
Source of funds	The study was funded by the Central Council for Research in Homeopathy		
Declared interests of study authors	Authors declared no conflicts of interest		
Setting / provider	Multi-centre research institutes in India		
Country(s) / region	India		
Enrolment period	Not reported		
Length of intervention + follow up	7 day intervention, 8 day follow up period		
Description of population	*N=*	*Description*	
participants	136	Adults with neck pain Inclusion criteria: Male and female patients between 30 and 60 years, with a chief complaint of neck pain including pain in the suboccipital and interscapular regions for the last 2 wks, having one or more episodes of neck pain and neck stiffness attack per mth on average for at least 3 mths with positive radiological findings for cervical spondylosis; pain intensity of minimum 4 as per Visual Analogue Scale (VAS), not on inflammatory or any other therapy in the past 1 wk.	
details	Exclusion criteria: Cervical myelopathy or radiculopathy; patients with neck pain and normal X-ray findings, patients taking physiotherapy, those having neck trauma/fracture/history of surgery/congenital spinal abnormalities, any systemic disease of bones and joints, other non specific lesions: acute neck strain, postural neck ache or whiplash injury, any systemic disease such as hypertension, diabetes mellitus, cardiovascular or cerebrovascular disease; inability to comply with the study protocol, alcoholics or drug users including psychiatric disease; pregnant and lactating women, patients deemed ineligible by an investigator and patients unwilling to sign the written informed consent form.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	67	Homeopathic treatments in 30c potency were selected based on acute totality. Three doses were given at 6 hour intervals daily, for 7 days
Intervention #2	--		

Characteristics of included studies	Neck pain					
Study ID	**Gupta 2020**					
Comparator #1 (control)	Placebo	69	Identical matching placebo was taken, 3 doses daily at 6 hour intervals for 7 days			
Comparator #2 (other)	--					
Comparator #3 (other)	--					
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Pain	Baseline and daily until end of study (day 8)	Visual analogy scale (VAS)	VAS Range: 0- 10 Higher is worse	
2	Primary	Stiffness	Baseline and daily until end of study (day 8)	Visual analogy scale (VAS)	VAS Range: 0- 10 Higher is worse	
3	Primary	Limitation of movement	Baseline and daily until end of study (day 8)	Cervical Spondylosis Pain Management Scale (CSPMS)	No further details provided	No further details provided for the CSPMS
4	Primary	Tenderness	Baseline and daily until end of study (day 8)	Cervical Spondylosis Pain Management Scale (CSPMS)	No further details provided	No further details provided for the CSPMS
5	Secondary	Quality of life	End of study (day 8)	Patient's Global Impression of Change Scale	Range: 0- 10 Higher is worse	
6	--	--				
Method of analysis						
Statistics	Independent sample t-tests and chi-squared tests were used to compare groups at baseline. The Friedman test was used for group differences at baseline, 3rd day and 8th day of follow up. Mann-Whitney test was used for analysing patient's global impression of change					
Population analysed	Per protocol	Drop-outs were not included in the analysis of the outcomes				
Missing data	Yes	2/136 participants had missing data				

Characteristics of included studies	Back pain		
Study ID	**Morris 2016**		
Study reference	Morris M, Pellow J, Solomon EM, Tsele-Tebakang T. Physiotherapy and a Homeopathic Complex for Chronic Low-back Pain Due to Osteoarthritis: A Randomized, Controlled Pilot Study. Alternative Therapies in Health & Medicine. 2016;22(1):48-56.		
Study design	RCT	Medication bottles (homeopathy and placebo) were numbered and randomised by an independent individual using a simple randomisation method. Participants selected a prenumbered bottle, thereby allocating themselves randomly.	
Author affiliation	3 authors are associated with a South African university and 1 author is a homeopath and physiotherapist		
Source of funds	University of Johannesburg, South Africa		
Declared interests of study authors	Authors declare no conflicts of interest		
Setting / provider	Private physiotherapy practice		
Country(s) / region	South Africa		
Enrolment period	Not specified		
Length of intervention + follow up	6 wks		
Description of population	*N=*	*Description*	
participants	30	Chronic lower back pain due to osteoarthritis	
details	Inclusion criteria: aged 45 to 75 years, symptomatic chronic lower back pain due to osteoarthritis for more than 3 mths as diagnosed by a health care practitioner, experienced symptoms of osteoarthritis, such as pain and decreased range of motion, as subjectively reported and by physical examination, and were receiving physiotherapy treatment from the identified physiotherapist. Exclusion criteria: receiving any form of therapy other than physiotherapy, had presented with acute lower back pain with the duration of 3 mths or less, were suffering from chronic lower back pain as a result of disc herniation, compression fracture, lumbar spinal stenosis, or other spondyloarthropathy.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Non-individualised	15	Homeopathic complex. 2 tablets, dissolved under the tongue, 20 minutes before meals, twice daily for 6 wks.
Intervention #2			

Characteristics of included studies	Back pain					
Study ID	**Morris 2016**					
Comparator #1 (control)	Placebo	15	Unmedicated lactose tablets that looked and tasted the same as the complex. 2 tablets, dissolved under the tongue, 20 minutes before meals, twice daily for 6 wks.			
Comparator #2 (other)						
Comparator #3 (other)						
Co-interventions	Physiotherapy treatment: all participants underwent a 30-minute session once every 2 wks that consisted of lower-back classic massage, mobilisation of lumbar joints, and the application of a heat pack					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Pain	1st, 2nd, 3rd, 4th consultations	Visual analogue scale (VAS)	0-10 Higher score worse	(change from baseline every two wks for 6 wks)
2	Secondary	Physical function/ mobility	1st, 2nd, 3rd, 4th consultations	Range of motion	Attraction-tape measurement Less range worse	(change from baseline every two wks for 6 wks)
3	Secondary	Disability/ function	1st, 2nd, 3rd, 4th consultations	Oswestry disability index	Score out of 100 Higher score is worse	(change from baseline every two wks for 6 wks)
4	Secondary	Medication use	1st, 2nd, 3rd, 4th consultations	Amount of pain medication needed		(change from baseline every two wks for 6 wks)
5	--	--				
6	--	--				
Method of analysis						
Statistics	The Shapiro-Wilk test was applied, which showed an abnormal distribution of data. Therefore, nonparametric tests were chosen for the analysis. The Friedman and Wilcoxon signed-ranks tests were used for intragroup analysis, and the Mann-Whitney U test and independent samples t test were used for intergroup analysis.					
Population analysed	Intent-to-treat	No participants excluded from analysis.				
Missing data	No	No participants lost to follow-up or discontinued intervention.				

Characteristics of included studies	Back pain		
Study ID	**Stam 2001**		
Study reference	Stam C, Bonnet MS, Van Haselen RA. The efficacy and safety of a homeopathic gel in the treatment of acute low back pain: A multi-centre, randomised, double-blind comparative clinical trial. British Homeopathic Journal. 2001;90(1):21-8.		
Study design	RCT	Randomisation software RCODE, in blocks of 4.	
Author affiliation	One author is affiliated with regulatory affairs in the Netherlands, two authors are affiliated with healthcare settings in the United Kingdom		
Source of funds	No information		
Declared interests of study authors	No information		
Setting / provider	General practitioner clinics in the United Kingdom		
Country(s) / region	United Kingdom		
Enrolment period	No information		
Length of intervention + follow up	1 wk (7 days)		
Description of population	*N=*	*Description*	
participants	161	Low back pain, acute	
details	Inclusion criteria: aged 18 to 65 years, acute attack of low back pain within previous 72 hours, free from low back pain during the previous three mths, at least moderately painful limitation of movement as determined by physical examination. Exclusion criteria: radicular symptoms indicating sacral/lumbar nerve root compression, location of pain above T12, rheumatoid arthritis, ankylosing spondylitis, known hypersensitivity to any of the components of both products, use of analgesics other than paracetamol during the treatment period, use of NSAIDs during the treatment period, receiving other treatment (physiotherapy, osteopathy, acupuncture, etc.) aimed at treating the acute low back pain during the treatment period, pregnancy, more than 96 hours elapsed since the onset of pain, including washout for analgesic and/or NSAIDs		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Non-individualised	83	SRL gel, homeopathic gel containing three homeopathic ingredients. 3 grams applied three times daily to the affected area. A spatula with a sticker indicating a dose of approximately 1g was used to measure the dose.
Intervention #2			

Characteristics of included studies	Back pain					
Study ID	**Stam 2001**					
Comparator #1 (control)	Active control	78	Cremor Capsici Compositus (CCC) topical medication. 3 grams applied three times daily to the affected area. A spatula with a sticker indicating a dose of approximately 1g was used to measure the dose.			
Comparator #2 (other)						
Comparator #3 (other)						
Co-interventions	Paracetamol 500mg tablets were provided as a rescue analgesic up to a maximum of eight tablets a day.					
Is comparator clearly inactive?	No	Comparison=other			Active control	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Pain	Change from baseline	Visual Analogue Scale (VAS)	Higher score is worse	Calculated as the difference between baseline and day 7
2	Primary	Pain	Change from baseline	Visual Analogue Scale (VAS)	Treatment success defined as at least 80% VAS reduction and 100% VAS reduction	
3	Secondary	Medication use	Measured at 7 days	Paracetamol use	Proportion of subjects using paracetamol	
4	Secondary	Working status	Measured at 7 days	Inability to work	Proportion of subjects still unable to work at the end of the study	
5	Secondary	Sleep	Measured at 7 days	Number of nights with disturbed sleep		
6	Secondary	Overall evaluation of efficacy	Measured at 7 days	Scale from excellent, good, fair, poor, useless, worse than useless	/ usefulness of product used	
Method of analysis						
Statistics	No information provided regarding specific statistical analyses, however analyses were performed at VSM Geneesmiddelen by using the program SPSS PC+ version 5.1					
Population analysed	Intent-to-treat	Intent-to-treat with all subjects who had a baseline VAS as well as at least one follow-up VAS were included in the primary efficacy parameters using the 'last-value-carried-forward' method.				
Missing data	Yes	6 subjects lost to follow up (2 intervention, 4 placebo)				

Characteristics of included studies	MENOPAUSAL SYMPTOMS		
Study ID	**Andrade 2019**		
Study reference	Andrade DCDS, Carmona F, Angelucci MA, Martinez EZ, Pereira AMS. Efficacy of a Homeopathic Medicine of Capsicum frutescens L(Solanaceae) in the Treatment of Hot Flashes in Menopausal Women: A Phase-2 Randomized Controlled Trial. Homeopathy: the Journal of the Faculty of Homeopathy. 2019;108(2):102-7. NCT01315041		
Study design	RCT		Patients were asked to take one flask of medicine from a box. The flasks were randomly numbered, and the allocation list was held by another researcher, not involved with patient recruitment or assessment. The allocation list (simple randomization) was generated through a website
Author affiliation	Authors were affiliated with universities in Brazil		
Source of funds	Authors reported none to declare		
Declared interests of study authors	Authors declared no conflicts		
Setting / provider	Outpatient clinic		
Country(s) / region	Brazil		
Enrolment period	September 2014 to November 2015		
Length of intervention + follow up	8 wk intervention		
Description of population	*N=*	*Description*	
participants	40	Women with menopausal hot flushes	
details	Inclusion criteria: Woman with menopausal hot flushes as major complaint, not having taken part in another clinical trial within the previous 6 mths, and not receiving any treatment for hot flushes or menopause, including anti-depressants. Exclusion criteria: Had any previous relationship with the researchers, history of hypersensitivity or dermatitis due to any kind of pepper, or haemorrhoids.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	MENOPAUSAL SYMPTOMS						
Study ID	**Andrade 2019**						
Intervention #1	Non-individualised	20	Participants received the homeopathic treatment of Malagueta taken orally, 5 drops, 3 times a day for 4 wks, then stop treatment for another 4 wks				
Intervention #2	--	--	--				
Comparator #1 (control)	Placebo	20	Placebo was an EtOH/H2O (30% w/v) solution without agitation, taken orally as described above				
Comparator #2 (other)	--	--	--				
Comparator #3 (other)	--	--	--				
Co-interventions	None reported						
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo		
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*	
1	Primary	Symptom severity	baseline (wk 0) and 1, 2, 4 and 8 wks	Measure yourself medical outcome profile (MYMOP)	Higher is worse		
2	Secondary	Level of activity	baseline (wk 0) and 1, 2, 4 and 8 wks	Measure yourself medical outcome profile (MYMOP)	Higher is worse		
3	Secondary	Quality of life	baseline (wk 0) and 1, 2, 4 and 8 wks	Measure yourself medical outcome profile (MYMOP)	Higher is worse		
4	--	--	--				
5	--	--	--				
6	--	--	--				

Characteristics of included studies	MENOPAUSAL SYMPTOMS	
Study ID	**Andrade 2019**	
Method of analysis		
Statistics	The treatment effects for the primary and secondary outcomes were determined by ordinal logistic models, adjusting for repeated measures. Calculated the mean difference between responses of the two groups and the odds ratio for response to treatment (defined as a reduction of at least three MYMOP categories) for the primary outcome, with corresponding 95% confidence intervals (95% CI), as estimates of effect size. A significance level of 5% was adopted	
Population analysed	Intent-to-treat	ITT specified
Missing data	Yes	7/40 participants withdrew from the study

Characteristics of included studies	MENOPAUSAL SYMPTOMS		
Study ID	**Colau 2012**		
Study reference	Colau JC, Vincent S, Marijnen P, Allaert FA. Efficacy of a non-hormonal treatment, BRN-01, on menopausal hot flashes: A multicenter, randomized, double-blind, placebo-controlled trial. Drugs in R and D. 2012;12(3):107-19. EUCTR2009-016959-21		
Study design	RCT	Computer generated random numbers. Key to randomisation kept in a sealed envelope until the end of the study	
Author affiliation	Authors were affiliated with Laboratoires Boirona and a hospital in France		
Source of funds	The study was funded by Laboratoires Boiron		
Declared interests of study authors	Not reported		
Setting / provider	Outpatient clinics		
Country(s) / region	France		
Enrolment period	June 2010 to July 2011		
Length of intervention + follow up	12 wk intervention		
Description of population	*N=*	*Description*	
participants	108	Women with menopausal hot flushes	
details	Inclusion criteria: Aged ≥50 years; had experienced amenorrhea for >12 mths; and if, during a routine gynaecologic consultation, they had spontaneously complained of hot flashes that had started <2 years previously and had significant repercussions on their social and/or professional life of ≥40 mm on a Visual Analog Scale (VAS) ranging from 0 to 100 mm, with a mean frequency of ≥5 hot flashes per day during the 48 hours preceding study enrolment. Exclusion criteria: Receiving or had ever received HRT; receiving or had received (within 2 wks prior to enrolment) b-alanine, food supplements (phytoestrogens, etc.), vitamin E, acupuncture aimed at relieving hot flashes, other homeopathic treatments aimed at relieving hot flashes; menopause induced artificially by surgery, chemotherapy, or radiotherapy; hot flashes that could be iatrogenic in origin or could be caused by an associated pathology; receiving antihypertensive treatment with clonidine, antidepressant treatment with SNRIs (venlafaxine), SSRIs, mirtazapine, or antiepileptic treatment with gabapentin		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	MENOPAUSAL SYMPTOMS					
Study ID	**Colau 2012**					
Intervention #1	Non-individualised	54	Participants were treated with a homeopathic remedy (BRN-01) in the form of oral tablets, taken twice daily for 12 wks			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	54	The placebo tablets were identical in appearance to the active tablets but included only saccharose (75%), lactose (24%), magnesium stearate E572 (1%), and purified water without any homeopathic dilutions. Dosing schedule as per the intervention arm			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Hot flush severity	Baseline (during the first 2 days after enrolment), every Tuesday and Wednesday until wk 11, then every day of wk 12	Hot flush score (HFS)	Lower is better	
2	Secondary	Quality of life	Baseline and end of treatment (12 wks)	Hot flush related daily interference scale (HFRDIS)	Lower is better	
3	Secondary	Symptom severity	Baseline and end of treatment (12 wks)	Menopause rating scale	Lower is better	
4	Secondary	Treatment adherence	End of treatment (12 wks)	Morisky-Green score	Higher is worse	
5	Secondary	Adverse events	End of treatment (12 wks)	Number of adverse events	Lower is better	
6	--	--	--			

Characteristics of included studies	MENOPAUSAL SYMPTOMS	
Study ID	**Colau 2012**	
Method of analysis		
Statistics	In the case of missing data, the analysis took into account the last evaluation available according to the last-observation-carried-forward (LOCF) technique. Qualitative data are described as the absolute and relative frequencies with 95% confidence intervals (CIs). Comparisons of means were carried out by analysis of variance (ANOVA) or by using the Kruskal-Wallis test if the distribution was not normal. Comparisons of percentages were carried out using the chi-squared test or Fisher's exact test if the conditions for use of the chi-squared test were not fulfilled	
Population analysed	Intent-to-treat	ITT specified, defined as all patients who took at least one dose of the treatment and had at least one post-enrolment evaluation
Missing data	Yes	7/108 participants withdrew from the study

Characteristics of included studies	MENOPAUSAL SYMPTOMS		
Study ID	**Gupta 2019**		
Study reference	Gupta J KD, Lamba CD, Gupta P, Shinde V, Wadhwa B, Soren A, Arya J S, Koley M, Pramanik A, Parveen S, Kumar A. Homoeopathic medicine –Sepia for the management of menopausal symptoms: A multicentric, randomised, double-blind placebo-controlled clinical trial. Indian Journal of Research in Homoeopathy. 2019;13 (4):219-28. CTRI/2011/12/002269		
Study design	RCT	Computer generated random numbers	
Author affiliation	Authors were affiliated with homeopathic research institutes in India		
Source of funds	The study was funded by the Central Council for Research in Homoeopathy, New Delhi under Ministry of AYUSH, Government of India		
Declared interests of study authors	Authors declared no conflicts		
Setting / provider	Multi-centre research centres		
Country(s) / region	India		
Enrolment period	April 2012 to September 2014		
Length of intervention + follow up	6 mth intervention and follow up		
Description of population	*N=*	*Description*	
participants	88	Women with menopausal symptoms	
details	Inclusion criteria: Perimenopausal women between 40 and 55 years of age with a history of menopausal symptoms for at least 1 mth within the last one year, signed the informed consent form, women presenting with indications for medicine – Sepia as per homoeopathic literature, receiving treatment for menopausal complaints or taking oral contraceptives in past 15 days, should not have been on HRT in past 2 mths. Exclusion criteria: Women with established menopause either natural or artificial, dysfunctional uterine bleeding/history of endometrial hyperplasia or malignancy, on long-term medication for any disease, history of severe psychiatric disturbance, history of systemic illnesses, hypertension, diabetes mellitus, cardio- or cerebro-vascular diseases, pelvic pathology requiring surgery or any malignancy and using any medicine or supplement containing oestrogen and progestin.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	MENOPAUSAL SYMPTOMS					
Study ID	**Gupta 2019**					
Intervention #1	Non-individualised	44	The homeopathic treatment Sepia 200c was prescribed at mthly intervals until end of treatment (6 mths)			
Intervention #2	--	--	--			
Comparator #1 (control)	Placebo	44	Identical placebo, taken at mthly intervals until end of treatment (6 mths)			
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptom severity	Baseline and mthly until end of treatment (6 mths)	Greene Climacteric scale (GCS)	Higher is worse	
2	Primary	Quality of life	Baseline and mthly until end of treatment (6 mths)	Utian Quality of Life (UQOL)	Higher is better	
3	--	--	--			
4	--	--	--			
5	--	--	--			
6	--	--	--			

Characteristics of included studies	MENOPAUSAL SYMPTOMS	
Study ID	**Gupta 2019**	
Method of analysis		
Statistics	Differences between groups analysed using independent t-tests. P < 0.05 was considered statistically significant	
Population analysed	Intent-to-treat	ITT presumed
Missing data	No	

Characteristics of included studies	MENOPAUSAL SYMPTOMS		
Study ID	**Jacobs 2005**		
Study reference	Jacobs J, Herman P, Heron K, Olsen S, Vaughters L. Homeopathy for menopausal symptoms in breast cancer survivors: A preliminary randomized controlled trial. Journal of Alternative and Complementary Medicine. 2005;11(1):21-7.		
Study design	RCT	Randomisation was done using computer-generated random numbers in blocks of 4 and 6 and was known only to the homeopathic pharmacist	
Author affiliation	Authors were affiliated with universities and a homeopathic clinic in the USA		
Source of funds	The study was funded by IDEA award # DAMD17-99-1-9438 from the U.S. Army Breast Cancer Research Project		
Declared interests of study authors	Not reported		
Setting / provider	Outpatient clinic		
Country(s) / region	Seattle, Washington, USA		
Enrolment period	1 December 1999 to 31 March 2001		
Length of intervention + follow up	1 year intervention and follow up		
Description of population	*N=*	*Description*	
participants	83	Breast cancer survivors with menopausal symptoms	
details	Inclusion criteria: Women with a history of carcinoma in situ or Stage I–III breast cancer who had completed all surgery, chemotherapy, and radiation treatment prior to enrolment in the study. Participants taking tamoxifen were included. Participants had a history of hot flashes for at least 1 mth, with an average of at least three hot flashes per day in the wk prior to beginning treatment. Exclusion criteria: Taking any other medications for the treatment of hot flushes and other associated symptoms, including specific vitamin regimens, herbs, estrogen or progestational agents, antidepressants, or sleep medications, concurrent chronic health problems such as rheumatoid arthritis, asthma, heart disease, and inflammatory bowel disease necessitating treatment with corticosteroids, expected to receive additional chemotherapy or radiation treatment within the next year, pregnancy or planning to become pregnant in the next year.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	MENOPAUSAL SYMPTOMS						
Study ID	**Jacobs 2005**						
Intervention #1	Individualised	26	Participants had a consultation with a homeopath and were prescribed an individualised treatment best matched to their symptoms. The prescription was sent to a homeopathic pharmacy who dispensed a placebo combination medicine and a verum single remedy. Dosing schedule was individualised, given mthly or every 2 mths.				
Intervention #2	Non-individualised	30	Participants had a consultation with a homeopath and dispensed a combination medicine of *Hyland's menopause* (over the counter homeopathic medication). One tablet taken orally, 3 times per day				
Comparator #1 (control)	Placebo	27	Participants had a consultation with a homeopath and were dispensed an identical placebo, one tablet taken orally, 3 times per day				
Comparator #2 (other)	--	--	--				
Comparator #3 (other)	--	--	--				
Co-interventions	None reported						
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis				Placebo	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*	
1	Primary	Hot flush severity	Baseline, 1, 2 3, 6, 9 and 12 mths	Hot flush frequency and severity by diary recording	Higher is worse		
2	Secondary	Hot flush frequency	Baseline, 1, 2 3, 6, 9 and 12 mths	Diary recording	Higher is worse		
3	Secondary	Symptom severity	Baseline, 1, 2 3, 6, 9 and 12 mths	Kupperman Menopausal index (KMI)	Higher is worse		
4	Secondary	Quality of life	Baseline, 1, 2 3, 6, 9 and 12 mths	SF-36	Higher is better		
5	--	--	--				
6	--	--	--				

Characteristics of included studies	MENOPAUSAL SYMPTOMS	
Study ID	**Jacobs 2005**	
Method of analysis		
Statistics	The chi-squared statistic was used to compare discrete descriptive characteristics between groups at entry into the study and analysis of variance (ANOVA) was used to compare continuous variables. Linear regression was used to determine the association between treatments and outcomes, controlling for other covariates as needed and generalized estimating equations (GEE) were used to accommodate the multiple observations per person.	
Population analysed	Intent-to-treat	ITT presumed
Missing data	Yes	28/83 participants had missing data

Characteristics of included studies	MENOPAUSAL SYMPTOMS		
Study ID	**Relton 2012**		
Study reference	Relton C, O'Cathain A, Nicholl J. A pilot 'cohort multiple randomised controlled trial' of treatment by a homeopath for women with menopausal hot flushes. Contemporary Clinical Trials. 2012;33(5):853-9. ISRCTN02875421		
Study design	RCT	A random numbers sheet was generated by the statistician on a one to one basis using a block randomisation procedure, with blocks of 8. The random numbers were put into sealed numbered envelopes	
Author affiliation	Authors were affiliated with the University of Sheffield, UK		
Source of funds	A pre-doctoral training fellowship award from the Department of Health's National Coordinating Centre for Research Capacity Development funded the authors' doctoral research and the feasibility study of the cmRCT design. All work has been independent from the funders in every way		
Declared interests of study authors	Not reported		
Setting / provider	Outpatient clinics		
Country(s) / region	North of England, UK		
Enrolment period	October 2005 to February 2007		
Length of intervention + follow up	36 wk intervention		
Description of population	*N=*	*Description*	
participants	48	Women with menopausal hot flushes	
details	Inclusion criteria: Aged 45–65, reported 14+ menopausal hot flushes/night sweats per wk, consented to study. Exclusion criteria: Taking HRT and not intending to stop, using immuno-suppressants or chemotherapy, homeopathy or acupuncture.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	MENOPAUSAL SYMPTOMS					
Study ID	**Relton 2012**					
Intervention #1	Individualised	24	Participants met with a homeopath up to 5 times throughout the study, and were prescribed individualised homeopathic treatments			
Intervention #2	--	--	--			
Comparator #1 (control)	Inactive control	48	The control was no intervention, participants did not receive any treatment or meet with a homeopath			
Comparator #2 (other)						
Comparator #3 (other)						
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Control (no intervention)	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Hot flush frequency and severity	Baseline and 36 wks post intervention	Hot flush frequency and severity scale	Higher is worse	
2	Secondary	Symptom severity	Baseline and 36 wks post intervention	Greene Climacteric scale	Range: 0-63 Higher is worse	
3	Secondary	Quality of life	Baseline and 36 wks post intervention	Measure yourself medical outcome profile (MYMOP)	Range: 0-6 Higher is worse	
4	Secondary	Symptom severity	Baseline and 36 wks post intervention	Measure yourself medical outcome profile (MYMOP)	Range: 0-6 Higher is worse	
5	Secondary	Quality of life	Baseline and 36 wks post intervention	EQ-5D	Range: 0-1 Higher is better	
6	Secondary	Medication use	Baseline and 36 wks post intervention	Medication change questionnaire	Lower is better	

Characteristics of included studies	MENOPAUSAL SYMPTOMS	
Study ID	**Relton 2012**	
Method of analysis		
Statistics	The methods and results of this pilot study were evaluated using an ITT analysis of all those with complete and analysable data	
Population analysed	Intent-to-treat	ITT specified, modified ITT conducted
Missing data	Yes	4/48 participants had missing data

Characteristics of included studies	MENOPAUSAL SYMPTOMS		
Study ID	**von Hagens 2012**		
Study reference	Von Hagens C, Schiller P, Godbillon B, Osburg J, Klose C, Limprecht R, et al. Treating menopausal symptoms with a complex remedy or placebo: A randomized controlled trial. Climacteric. 2012;15(4):358-67. NCT00152776		
Study design	RCT	Lists for stratified randomised allocation to the three treatment groups with block length of 6 were created by an independent biometrician	
Author affiliation	Authors were affiliated with the University of Heidelberg and an institute for naturopathy and Chinese medicine in Heidelberg, Germany		
Source of funds	WALA Heilmittel GmbH, Bad Boll/Eckwälden, the manufacturer of the medication, funded the study, provided the properly labelled study medication and weighed the remaining medication to allow determination of adherence to dosing instruction		
Declared interests of study authors	Authors declared no conflicts		
Setting / provider	Outpatient clinic		
Country(s) / region	Heidelberg, Germany		
Enrolment period	February 2005 to March 2006		
Length of intervention + follow up	36 wk follow up. 3 x 12 wk intervention periods		
Description of population	*N=*	*Description*	
participants	102	Women with menopausal symptoms	
details	Inclusion criteria: Requested treatment of menopausal symptoms, had a total score of ≥ 3 on the Menopause Rating Scale (MRS II), were aged ≥ 45 years, were able to communicate in the German language and presented with normal pap smear not older than 12 mths before screening Exclusion criteria: Hormone therapy during the past 2 mths before recruitment, use of other complementary and alternative treatments 7 days before and during participation in the trial, menopausal symptoms induced by surgery, chemotherapy or endocrine therapy for cancer, pregnancy, participation in another clinical trial until 4 wks before recruitment, inability to communicate, allergy to trial remedy, bee allergy		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	MENOPAUSAL SYMPTOMS		
Study ID	**von Hagens 2012**		
Intervention #1	Non-individualised	33	Participants received a homeopathic treatment consisting of globuli velati made of saccharose coated with Apis regina tota GI Dil. D4 0.1 g (HAB, Method 41c), Argentum metallicum Dil. D5 0.1 g and Ovaria bovis GI Dil. D4 0.1 g (HAB, Method. 41a) per 10 g (Ovaria comp. Globuli velati ™ compounded according to the pharmacopoeia homeopathica (HAB, Method 39c) or identical placebo made of saccharose only. Taken orally, 3 x 10 globuli/day. An interim visit or telephone call at 6, 18 and 30 wks was planned. Homeopathy treatment was taken for the first 24 wks, then placebo was taken for the next 12 wks.
Intervention #2	Non-individualised	34	Treatment is as described above, however homeopathy is taken for the first 12 wks, then placebo for 12 wks, followed by homeopathy again for another 12 wks.
Comparator #1 (control)	Placebo	35	Treatment is as described above, however placebo is taken for the first 12 wks, then homeopathy for the following 24 wks.
Comparator #2 (other)			
Comparator #3 (other)			
Co-interventions	None reported		
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis	Placebo

Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Symptom severity	Baseline, 12 wks, 24 wks and 36 wks	Menopause rating scale (MRS II) - Total score	Higher is worse	
2	Secondary	Adverse events	Baseline, 12 wks, 24 wks and 36 wks	Number of adverse events	Higher is worse	
3	Secondary	Medication adherence	Baseline, 12 wks, 24 wks and 36 wks	Number and proportion of missing doses	Higher is worse	
4	--	--	--			
5	--	--	--			
6	--	--	--			

Characteristics of included studies	MENOPAUSAL SYMPTOMS	
Study ID	**von Hagens 2012**	
Method of analysis		
Statistics	Confirmatory analysis was done by a two-sided t-test with a type I error rate of α = 5%. Main analysis was done based on the full analysis set (FAS) according to the ITT principle. The FAS involved all randomised patients that received at least one dose of the study medication and had the primary efficacy endpoint documented. All statistical tests were carried out as two-sided. Concerning the analyses of secondary endpoints, no adjustment for multiple testing was done. Therefore, p values for secondary endpoints are considered as descriptive	
Population analysed	Other (provide details)	ITT and per-protocol analysis methods were used
Missing data	Yes	18/102 participants had missing data that were not analysed at the end of the first study period (12 wks)

Characteristics of included studies	MENSTURAL DISORDERS, Dysmenorrhea		
Study ID	**Charandabi 2016**		
Study reference	Charandabi, S. M. A., Biglu, M. H., & Rad, K. Y. (2016). Effect of homeopathy on pain intensity and quality of life of students with primary dysmenorrhea: A randomized controlled trial. Iranian Red Crescent Medical Journal, 18(9) (no pagination), Article e30902. https://doi.org/https://dx.doi.org/10.5812/ircmj.30902		
Study design	RCT		An independent person who was not involved in participant recruitment and data collection determined the allocation sequence using a computer program considering block randomisation with randomly unequal block sizes of 4 and 6
Author affiliation	The authors are affiliated with a university in Iran		
Source of funds	Grant from the Tabriz University of Medical Sciences		
Declared interests of study authors	Not reported		
Setting / provider	Female dormitories of the Tabriz University of Medical Sciences		
Country(s) / region	Iran		
Enrolment period	December 2013 to April 2014		
Length of intervention + follow up	2 mths pre-intervention + 2 mths post-intervention		
Description of population	*N=*	*Description*	
participants	54	Women with dysmenorrhea	
details	Inclusion criteria: Regular menstrual periods, having moderate or severe primary dysmenorrhea (pain score of 4 to 9 on a 10-cm visual analogue scale [VAS]) in the recent cycles), having no prior experience of homeopathy, being single, and age 18 o 27 years Exclusion criteria: History of any chronic diseases or allergy, smokers, those using oral contraceptive pills or corticosteroids or having a history of their use in the previous 6 mths		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	27	Homeopathic remedy administered at each visit to homeopaths private office (twice between the 8th to 12th days of menstrual cycle with 1 mth interval)
Intervention #2	--	--	--
Comparator #1 (control)	Placebo	27	As per intervention with identical placebo (lactose pill)

Characteristics of included studies	MENSTURAL DISORDERS, Dysmenorrhea				
Study ID	**Charandabi 2016**				
Comparator #2 (other)	--	--	--		
Comparator #3 (other)	--	--	--		
Co-interventions	None reported				
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis		Placebo	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Pain intensity	Baseline, first and second cycle post-intervention	Visual analogue scale (VAS)	Range: 0-10 Higher is worse
2	Primary	Quality of life	Baseline, post intervention	Short-form 36 (SF-36)	Range: 0-100 Higher is better
3	Secondary	Medication use	Baseline, first and second cycle post-intervention	Number of analgesic pills taken at each cycle	Range: 0-100 Lower is better
4	--	--	--	--	--
5	--	--	--	--	--
Method of analysis					
Statistics	Kolmogorov-Smirnov (K-S) test; ANOVA; ANCOVA; sample t-test; Wilcoxon signed-rank test				
Population analysed	Intent-to-treat	Modified ITT			
Missing data	Yes	7/54 participants lost to follow up (6 from placebo and 1 from homeopathy group)			

Characteristics of included studies	MENSTURAL DISORDERS, Premenstrual syndrome		
Study ID	**Klein-Laansma 2017**		
Study reference	Klein-Laansma CT, Jong M, von Hagens C, Jansen J, van Wietmarschen H, Jong MC. Semi-Individualized Homeopathy Add-On Versus Usual Care Only for Premenstrual Disorders: A Randomized, Controlled Feasibility Study. J Altern Complement Med. 2018;24(7):684-93. NTR3560		
Study design	RCT		Computer generated random numbers by a third party
Author affiliation	Authors were affiliated with a university in Sweden, a hospital in Germany and the department of health and nutrition in the Netherlands		
Source of funds	The study was funded by the International Scientific Committee for Homeopathic Investigations (ISCHI), the Swedish Scientific Homeopathic Association, the Hilly de Roever Bonnet Fund and the Royal Dutch consumers association for homeopathy (KVHN)		
Declared interests of study authors	Authors declared no competing financial interests		
Setting / provider	General and private homeopathic practices in the Netherlands and Sweden, and an outpatient clinic in Germany		
Country(s) / region	Multiple; the Netherlands, Sweden and Germany		
Enrolment period	October 2012 to 2016		
Length of intervention + follow up	4 mth intervention		
Description of population	*N=*	*Description*	
participants	60	Women with premenstrual syndrome and premenstrual disorder	
details	Inclusion criteria: Women aged 18–50 years and diagnosed as having PMS according to the International Classification for Primary Care (ICPC-2) or PMDD according to the Diagnostic Statistic Manual (DSM-IV) criteria based on prospective daily rating of symptoms during two complete menstrual cycles. Exclusion criteria: Major psychiatric comorbidity or physical comorbidity with large impact on general health		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	28	Participants had consultations with a homeopath and were prescribed individual treatment based on a patient questionnaire
Intervention #2	--	--	--
Comparator #1 (control)	Inactive control	32	Control (no intervention)

Characteristics of included studies	MENSTRUAL DISORDERS, Premenstrual syndrome				
Study ID	**Klein-Laansma 2017**				
Comparator #2 (other)	--	--	--		
Comparator #3 (other)	--	--	--		
Co-interventions	Usual care, provided by the participants' general practitioner according to their preferences				
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis		Control (no intervention)	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Symptom severity	Baseline and end of study (4 mths)	Daily record of severity of problems (DRSP)	Range: 168 to 1008 Higher is worse
2	Secondary	Symptom severity	Baseline and end of study (4 mths)	Premenstrual tension syndrome self-rating (PMTS-VAS)	Range: 0-100 Higher is worse
3	Secondary	Quality of life	Baseline and end of study (4 mths)	Measure yourself concern and wellbeing (MYCAW) questionnaire	Range: 0-6 Higher is worse
4	Secondary	Safety	End of study (4 mths)	Number of adverse events	Higher is worse
5	--	--	--	--	--
Method of analysis					
Statistics	Mean changes between groups were compared using t-tests. Effect sizes were expressed using Cohen's *d* . Significance of the differences was determined using t-tests or Kruskal–Wallis rank-sum tests for non-normal distribution				
Population analysed	Other (provide details)	ITT analysis was performed for primary outcome measures regarding effect size calculation, including all randomized women who had start. All other analyses were performed as per protocol, including all women who had executed the intervention as described in the study protocol			
Missing data	Yes	14/60 participants had missing data			

Characteristics of included studies	MENSTURAL DISORDERS, Dysmenorrhea		
Study ID	**Singh 2020**		
Study reference	CTRI/2018/07/014949		
Study design	RCT	Computer generated random numbers (simple random sampling method)	
Author affiliation	Authors were affiliated with a homeopathic hospital and research centre in India		
Source of funds	Not reported		
Declared interests of study authors	Authors declared no conflicts		
Setting / provider	Trial conducted at a homeopathic hospital and research institute		
Country(s) / region	Sri Ganganagar Rajasthan, India		
Enrolment period	July 2018 to January 2020		
Length of intervention + follow up	Study duration was 18 mths. Outcome results measured at 6 mths		
Description of population	*N=*	*Description*	
participants	65	Women with dysmenorrhoea	
details	Inclusion criteria: Meet case definition of primary dysmenorrhoea, ages 12-25, willing to participate and adhere to requirements of study. Exclusion criteria: Not meeting definition of primary dysmenorrhoea, patients requiring emergency medical intervention, not consenting, non-adherence to study requirements.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	30	Participants received homeopathic treatment based on totality of symptoms
Intervention #2	--	--	--
Comparator #1 (control)	Placebo	35	Placebo in similar form to treatment

Characteristics of included studies	MENSTURAL DISORDERS, Dysmenorrhea					
Study ID	**Singh 2020**					
Comparator #2 (other)	--					
Comparator #3 (other)	--					
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	
1	Primary	Pain	Baseline and end of treatment (6 mths)	VAS	Range: 0-100 Higher is worse	
2	--	--	--	--	--	
3	--	--	--	--	--	--
4	--	--	--	--	--	--
5	--	--	--	--	--	
Method of analysis						
Statistics	Normality of data was checked using the Kolmogoriv- Smirnov Test (K-S Test). Mann Whitney U test was applied (as data was not normally distributed). P < 0.05 two tailed statically significant.					
Population analysed	Intent-to-treat	ITT specified and conducted				
Missing data	Yes	1/64 participants withdrew from the study				

Characteristics of included studies	MENSTURAL DISORDERS, Endometriosis		
Study ID	**Teixeira 2016**		
Study reference	Teixeira MZ, Podgaec S, Baracat EC. Potentized estrogen in homeopathic treatment of endometriosis-associated pelvic pain: A 24-wk, randomized, double-blind, placebo-controlled study. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2017;211:48-55.		
Study design	RCT		Randomisation sequence was created by an independent supervisor using a random number generator. Both physician-investigator and participants were blinded
Author affiliation	Authors were affiliated with a university and hospital in Sao Paulo, Brazil		
Source of funds	Authors declared there was no funding source		
Declared interests of study authors	Authors declared no conflicts		
Setting / provider	Endometriosis unit of a clinical hospital in the University of Sao Paulo		
Country(s) / region	Sao Paulo, Brazil		
Enrolment period	2014 to unknown		
Length of intervention + follow up	24 wk intervention		
Description of population	*N=*	*Description*	
participants	50	Women with endometriosis	
details	Inclusion criteria: Aged 18-45 years, diagnosis of deeply infiltrating endometriosis based on clinical history and demonstration of lesions on MRI or TVU after bowel preparation, absence of clinical or laboratory signs of menopause or premature ovarian failure, presence of chronic pelvic pain refractory to conventional therapy (one year at least), score ≥5 on a visual analogue scale for endometriosis associated pelvic pain Exclusion criteria: not reported		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Non-individualised	23	Participants were given homeopathic potencies of estrogen administered every 8 wks (for 24 wks) in the form of three oral drops administered twice daily (every 12 hours). Estrogen potency of 12cH was administered on visit 1, 18cH on visit 2 and 24cH on visit 3.
Intervention #2	--	--	--
Comparator #1 (control)	Placebo	27	Participants were given identical vials containing hydroalcoholic solution only, same scheduling as the intervention group

Characteristics of included studies	MENSTURAL DISORDERS, Endometriosis					
Study ID	**Teixeira 2016**					
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	
1	Primary	Pain	Baseline, wk 8, wk 16 and end of study (wk 24)	Visual analogue scale (VAS) - Global EAPP score	Range: 0-50 Higher is worse	
2	Secondary	Quality of life	Baseline and end of study (24 wks)	SF-36 Health survey questionnaire	Higher is better	
3	Secondary	Depression	Baseline and end of study (24 wks)	Beck depression inventory (BDI)	Range: 0-63 Higher is worse	
4	Secondary	Anxiety	Baseline and end of study (24 wks)	Beck anxiety inventory (BAI)	Range: 0-63 Higher is worse	
5	--	--	--	--	--	--
Method of analysis						
Statistics	Comparison between groups and time points was performed by means of generalised estimating equations with first-order autoregressive structure, normal marginal distribution and identity link function. Outcome measures that showed statistical significance were subjected to Bonferroni test to establish between which groups and time-points differences in symptoms and scales occurred					
Population analysed	Other (provide details)	Data were subjected to ITT analysis and per-protocol analysis				
Missing data	Yes	9/50 participants had missing data				

Characteristics of included studies	MENSTURAL DISORDERS, Premenstrual syndrome		
Study ID	**Yakir 1994**		
Study reference	Yakir M, Kreitler S, Oberbaum M, Bzizinsky A, Vithoulkas G, Bentwich Z. Homeopathic treatment of premenstrual syndrome: a pilot study. Unpublished: 8th GIRI Meeting, Jerusalem Israel, December 1994. 1994:49-50. Yakir M, Kreitler S, Brzezinski A, Vithoulkas G, Oberbaum M, Bentwich Z. Effects of homeopathic treatment in women with premenstrual syndrome: A pilot study. British Homeopathic Journal. 2001;90(3):148-53.		
Study design	RCT	Medications were encoded prior to the study by random permutation method, performed by a third party	
Author affiliation	Two authors are affiliated with two Israeli universities; one author is from Greece; two authors are affiliated with medical centres/hospitals in Israel		
Source of funds	The study was funded by independent's; G Vithoulkas and S Corub; and by the Deutsche Homeopathie Union		
Declared interests of study authors	No information		
Setting / provider	Gynae logical Outpatient Clinic of Hasdassah University Hospital		
Country(s) / region	Israel		
Enrolment period	1992 to 1994		
Length of intervention + follow up	2 mth baseline assessment with post-intervention follow up for 3 mths		
Description of population	*N=*	*Description*	
participants	23	Women with premenstrual syndrome (PMS)	
details	Inclusion criteria: No other significant physical or mental problem, diagnosis of PMS according to accepted criteria, aged 20-50, symptomatology corresponding of one of five homeopathic drugs Exclusion criteria: Not meeting the inclusion criteria or not prepared to fill out questionnaires daily for 5 mths		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	13	1g dose of homeopathic preparation in 200c potency prepared in lactose globules administered orally once, on the seventh day after the start of the period
Intervention #2	--	--	--
Comparator #1 (control)	Placebo	10	As per intervention with identical placebo

Characteristics of included studies	MENSTURAL DISORDERS, Premenstrual syndrome				
Study ID	**Yakir 1994**				
Comparator #2 (other)			--		
Comparator #3 (other)			--		
Co-interventions	None reported				
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Symptom severity	baseline (mth 0), at intervention (2 mths), followup (5 mths)	Menstrual distress questionnaire (MDQ)	Higher is worse
2	Secondary	Overall PMS effect	baseline (mth 0), at intervention (mths 1, 2 & 3), followup (5 mths)	Self assessment on a scale from 0 to 4	Higher is worse
3	Secondary	Relative improvement rate	baseline (mth 0), at intervention (2 mths), followup (5 mths)	Number and % of women improved and by what magnitude	Higher number, percentage and improvement ratio means better effect
4	Secondary	Medication use	Daily dairy	Medication consumption in the 7 day period prior to menses	Higher is worse
5	Secondary	Anxiety	baseline (mth 0), at intervention (2 mths),	Taylors manifest anxiety scale	
Method of analysis					
Statistics	Results were coded for SPSS software. Non parametric statistics were used, due to small group size and non-normal distribution.				
Population analysed	Intent-to-treat	Modified-ITT			
Missing data	Yes	4/23 participants had missing data			

Characteristics of included studies	MENSTURAL DISORDERS, Premenstrual syndrome		
Study ID	**Yakir 2019**		
Study reference	Yakir M, Klein-Laansma CT, Kreitler S, Brzezinski A, Oberbaum M, Vithoulkas G, et al. A Placebo-Controlled Double-Blind Randomized Trial with Individualized Homeopathic Treatment Using a Symptom Cluster Approach in Women with Premenstrual Syndrome. Homeopathy: the Journal of the Faculty of Homeopathy. 2019;108(4):256-69		
Study design	RCT		Computer generated random numbers. Codes concealed until after termination of study
Author affiliation	Authors were affiliated with homeopathy or complementary medicine associations in Israel and Greece, hospital and research centres in Israel, health and nutrition institute in the Netherlands and Rosetta Genomics in Israel		
Source of funds	The study was supported by grants from the Deutsche Homöopathische Union (DHU), Karlsruhe, Germany, the EtzHatamar Fund, Israel, and Stichting VHAN, Bunnik, Netherlands.		
Declared interests of study authors	The authors declare no competing financial interests. One author reports personal fees from the Deutsche Homöopathische-Union (DHU), Karlsruhe, Germany, outside the submitted work		
Setting / provider	Outpatient clinic		
Country(s) / region	Jerusalem, Israel		
Enrolment period	1996 to 1999		
Length of intervention + follow up	3 mth follow up		
Description of population	*N=*	*Description*	
participants	105	Women with premenstrual syndrome (PMS)	
details	Inclusion criteria: Aged 20 - 50 years, PMS persistent for more than 1 year and confirmed by the menstrual distress questionnaire (MDQ), provided consent, symptoms matching symptom profile of predetermined homeopathic medicines. Exclusion criteria: Had participated in the pilot study, concomitant health disorders and regular use of medications (except incidental medication for premenstrual symptoms).		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	49	Participants met with a homeopath and were prescribed a treatment based on their symptom profile. Treatment was in 200c potency, taken once on day 7 of their next menstruation. There were no follow up consultations of repetitions in treatment.
Intervention #2	--	--	--
Comparator #1 (control)	Placebo	56	Participants received an equivalent placebo with the same treatment schedule

Characteristics of included studies	MENSTURAL DISORDERS, Premenstrual syndrome					
Study ID	**Yakir 2019**					
Comparator #2 (other)	--	--	--			
Comparator #3 (other)	--	--	--			
Co-interventions	None reported					
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	
1	Primary	Symptom severity	baseline (mth 0), at intervention (mths 1, 2 & 3), followup (6 mths)	Menstruation distress questionnaire (MDQ)	Higher is worse	
2	Secondary	Medication use	baseline (mth -1), at intervention (mths 1, 2 & 3), followup (6 mths)	Mean self-reported drug consumption in the 12 premenstrual days	Higher is worse	
3	Secondary	Absenteeism	baseline (mth -2), at intervention (mths 1, 2 & 3), followup (6 mths)	Number of sick days during the 12 premenstrual days	Higher is worse	
4	--	--	--	--	--	--
5	--	--	--	--	--	--
Method of analysis						
Statistics	Multivariate analysis was performed by either the general linear model (mixed models) conducted with repeated measures or one-way analysis of variance (ANOVA) for measuring changes over time with several variables. One-way tests were performed when changes in one direction could be assumed. T-tests were used for comparing two categories of means. Proportions were compared by using chi-squared tests. Associations were measured with Pearson's correlation test.					
Population analysed	Intent-to-treat	ITT specified, modified ITT and per-protocol analysis used				
Missing data	Yes	9/105 participants withdrew from the study				

Characteristics of included studies	Chronic fatigue		
Study ID	**McKendrick 1999**		
Study reference	McKendrick M. Chronic fatigue syndrome: a controlled trial of the efficacy of homeopathic treatment. National Research Register. 1999. Weatherley-Jones E, Thomas K. A randomised, controlled trial of homeopathic treatment for chronic fatigue syndrome. 17th annual meeting of the international society of technology assessment in health care: building bridges between policy, providers, patients and industry; 2001 june 3-6. 2001:67. Stanley PJ. Chronic fatigue syndrome: A controlled trial of the efficacy of homeopathic treatment. National Research Register. 2001. Weatherley-Jones E, Nicholl JP, Thomas KJ, Parry GJ, McKendrick MW, Green ST, et al. A randomized, controlled, triple-blind trial of the efficacy of homeopathic treatment for chronic fatigue syndrome. Journal of Psychosomatic Research. 2004;56(2):189-97.		
Study design	RCT	Statistician computer-generated randomisation sequence. No contact between homeopaths and the pharmacy dispencing treatment or placebo.	
Author affiliation	The authors were affiliated with universities and hospitals in the UK		
Source of funds	Grant from the Linbury Trust		
Declared interests of study authors	No information		
Setting / provider	Community, patients recruited from outpatient departments		
Country(s) / region	UK, Leeds and Sheffield		
Enrolment period	February 2006 to September 2008		
Length of intervention + follow up	6 mth intervention, outcomes measured 7 mths after randomisation		
Description of population	*N=*	*Description*	
participants	103	Chronic fatigue syndrome	
details	Inclusion criteria: aged 18 or older, Oxford criteria for CFS, severe disabling fatigue affecting physical and mental functioning, present for at least 6 mths for which physical causes of chronic fatigue have been excludedno clinically significant abnormalities in blood test Exclusion criteria: currently engaged in individual conselling or psychotherapy, in clinical trials for CFS, pregnant, currently receiving homeopathic treatment, currently receiving cognitive behavioural therapy.		
Description of intervention/comparator	Type of intervention	*n=*	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*
Intervention #1	Individualised	53	Individualised homeopathy, mthly consultations with a homeopath for 6 mths, most frequently single products, however there were no limitations on product, dosage or potency reported
Intervention #2	--	--	--
Comparator #1 (control)	Placebo	50	Placebo. Participants also received homeopathic consultation, however were dispenced placebo medication by a homeopathic pharmacy.
Comparator #2 (other)	--	--	--

Characteristics of included studies	Chronic fatigue					
Study ID	**McKendrick 1999**					
Comparator #3 (other)	--	--	--			
Co-interventions	All participants receive homeopathic consultation to determine the most appropriate medicinal product					
Is comparator clearly inactive?	Yes	Comparison=control	Placebo			
Outcomes (meaure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*	*other*
1	Primary	Fatigue	Baseline, post intervention (6 mths)	Multidimensional Fatigue Inventory - general fatigue	Scores range 4-20	
2	Primary	Fatigue	Baseline, post intervention (6 mths)	MFI - physical fatigue	Scores range 4-20	
3	Primary	Fatigue	Baseline, post intervention (6 mths)	MFI - mental fatigue	Scores range 4-20	
4	Primary	Fatigue	Baseline, post intervention (6 mths)	MFI - reduced activity	Scores range 4-20	
5	Primary	Fatigue	Baseline, post intervention (6 mths)	MFI - reduced motivation	Scores range 4-20	
6	Secondary	Fatigue Impact	Baseline, post intervention (6 mths)	Fatigue Impact Scale - cognitive	Higher score is worse	
7	Secondary	Fatigue Impact	Baseline, post intervention (6 mths)	FIS - physical	Higher score is worse	
8	Secondary	Fatigue Impact	Baseline, post intervention (6 mths)	FIS - social	Higher score is worse	
9	Secondary	Health-related quality of life	Baseline, post intervention (6 mths)	Functional Limitations Profile - physical	Higher score is worse	Scores calculated as percentage
10	Secondary	Health-related quality of life	Baseline, post intervention (6 mths)	Functional Limitations Profile - psychosocial	Higher score is worse	Scores calculated as percentage
11	Secondary	Psychcological wellbeing	Baseline, post intervention (6 mths)	General Health Questionnaire - 28	Higher score is worse. 28-items	Scoring methods vary
Method of analysis						
Statistics	Mean post-treatment scores were compared between groups using analysis of covariance with the baseline pre-treatment score as the covariate. Proportions of people in each group experiencing a clinically meaningful change were compared using chi-square statistics.					
Population analysed	Intent-to-treat	ITT specified				
Missing data	Yes	17/103 participants were lost to follow up. Participants who returned post-treatment outcome measures with items missing had missing items imputed using simple mean imputation. Participants who did not return post-treatment scores were excluded from the analysis.				

Characteristics of included studies	Fibromyalgia		
Study ID	**Bell 2004**		
Study reference	Bell IR, Lewis DA, 2nd, Brooks AJ, Schwartz GE, Lewis SE, Caspi O, et al. Individual differences in response to randomly assigned active individualized homeopathic and placebo treatment in fibromyalgia: implications of a double-blinded optional crossover design. Journal of Alternative & Complementary Medicine. 2004;10(2):269-83. Bell IR, Lewis DA, Brooks AJ, Schwartz GE, Lewis SE, Walsh BT, et al. Improved clinical status in fibromyalgia patients treated with individualized homeopathic remedies versus placebo. Rheumatology. 2004;43(5):577-82. Bell IR, Lewis DA, 2nd, Schwartz GE, Lewis SE, Caspi O, Scott A, et al. Electroencephalographic cordance patterns distinguish exceptional clinical responders with fibromyalgia to individualized homeopathic medicines. Journal of Alternative & Complementary Medicine. 2004;10(2):285-99. Bell IR, Lewis IDA, Lewis SE, Schwartz GE, Brooks AJ, Scott A, et al. EEG alpha sensitization in individualized homeopathic treatment of fibromyalgia. International Journal of Neuroscience. 2004;114(9):1195-220.		
Study design	RCT	Computer generated random numbers. Only methodologist had access to code.	
Author affiliation	Authors were affiliated with a university in the US		
Source of funds	This study was supported by NIH grants R21 AT00315 (IRB), K24 AT00057 (IRB), P20 AT00774 (GES), P50 AT00008 from the National Institutes of Health National Center for Complementary and Alternative Medicine (NCCAM) and NIH HL53938–07S1 (CMB).		
Declared interests of study authors	The authors declared no conflict of interest		
Setting / provider	Community		
Country(s) / region	Arizona, US		
Enrolment period	Not reported		
Length of intervention & follow up	4 mth intervention with option crossover after 4 mths. Outcomes reported after 3 mths.		
Description of population	*N=*	*Description*	
participants	62	Physician diagnosed fibromyalgia	
details	Inclusion criteria: Non-pregnant female and males with a prior physician diagnosis of fibromyalgia (confirmed on rheumatological physical examination using the 1990 American College of Rheumatology criteria), stable conventional medication doses for at least 2 mths prior to enrolment, score to criteria for fibromyalgia on a 15-item, 4-point Likert symptom screening questionnaire. Exclusion criteria: History of alcohol or drug abuse, steroid use, current narcotic analgesic, benzodiazepine or antihypertensive medication use or nasal trauma, anaphylaxis history, diabetes, serious neurological, heart, lung, liver or kidney disease, psychosis and active suicidality.		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Fibromyalgia				
Study ID	**Bell 2004**				
Intervention #1	30	Individualised	Participants had visits with a homeopath every 2 mths for 6 mths, with optional crossover after 4 mths. LM potency, taken orally, gradually raised over course of treatment.		
Intervention #2	--	--	--		
Comparator #1 (control)	32	Placebo	Homeopathic pharmacy dispensed homeopathy or placebo in identical bottles. Patients on placebo also received homeopathic visits.		
Comparator #2 (other)	--	--	--		
Comparator #3 (other)	--	--	--		
Co-interventions	None reported				
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis		Placebo	
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Fibromyalgia symptoms	Baseline, 3 mths, 6 mths	Tender point count	Range: 0-18 Higher is worse
2	Primary	Pain	Baseline, 3 mths, 6 mths	Tender point pain on palpation exam	Range: 0-180 Higher is worse
3	Primary	Pain	Baseline, 3 mths, 6 mths	McGill Affective Pain	Range: 0-12 Higher is worse
4	Primary	Pain	Baseline, 3 mths, 6 mths	McGill Sensory Pain	Range: 0-33 Higher is worse
5	Primary	Fibromyalgia symptoms	Baseline, 3 mths, 6 mths	Appraisal of fibromyalgia	Range: 7-35 Higher is worse
6	Primary	Emotional wellbeing	Baseline, 3 mths, 6 mths	POMS fatigue	Range: 0-28 Higher is worse

Characteristics of included studies	Fibromyalgia				
Study ID	**Bell 2004**				
7	Primary	Emotional wellbeing	Baseline, 3 mths, 6 mths	POMS depression	Range: 0-60 Higher is worse
8	Primary	Emotional wellbeing	Baseline, 3 mths, 6 mths	POMS anger-hostility	Range: 0-48 Higher is worse
9	Primary	Health-related quality of life	Baseline, 3 mths, 6 mths	Global health rating	Range: 3-15 Higher is better
7	Secondary	Central nervous system function	Baseline and 3 mths	EEG	EEG alpha magnitude and cordance
8	Secondary	Physical wellbeing	Baseline and 3 mths	Functional Assessment of Chronic Illness Therapy (FACIT)	Range not specified Higher is better
9	Secondary	Emotional wellbeing	Baseline and 3 mths	FACIT	Range not specified Higher is better
10	Secondary	Functional wellbeing	Baseline and 3 mths	FACIT	Range not specified Higher is better
11	Secondary	Social-family wellbeing	Baseline and 3 mths	FACIT	Range not specified Higher is better
12	Secondary	Spiritual wellbeing	Baseline and 3 mths	FACIT	Range not specified Higher is better
Method of analysis					
Statistics	Active and placebo groups compared with one-way analyses of variance and chi-squared tests for differences in baseline demographics and clinical status. For analyses of covariance they used baseline values of a given outcome variable and variables on which the groups differed at P < 0.1 or better as covariates. Groups were compared using general linear model statistics, first without and then adjusted with appropriate covariates.				
Population analysed	Intent-to-treat	Specified ITT, participants without follow up data were not analysed			
Missing data	Yes	9/62 participants withdrew from the study. Those with missing follow up data were excluded from the analysis.			

Characteristics of included studies	Fibromyalgia		
Study ID	**Fisher 1988**		
Study reference	Fisher P. Rhus toxicodendron in the treatment of fibromyalgia: a double-blind, placebo-controlled trial, with cross-over. J Omhi. 1988;1(3):26-8. Fisher P, Greenwood A, Huskisson EC, Turner P, Belon P. Effect of homeopathic treatment on fibrositis (primary fibromyalgia). BMJ (Clinical research ed). 1989;299(6695):365-6.		
Study design	quasi RCT	Patients received treatment and placebo for one mth each in random sequence. Method of randomisation not specified.	
Author affiliation	Authors were affiliated with a hospital in London and a research laboratory in France		
Source of funds	Source of funds not reported by study authors		
Declared interests of study authors	Not reported		
Setting / provider	Outpatient clinic		
Country(s) / region	London, UK		
Enrolment period	Not reported		
Length of intervention & follow up	1 mth intervention/placebo with crossover at 1 mth. Outcomes reported at the end of active and placebo treatment periods		
Description of population	*N=*	*Description*	
participants	30	Met diagnostic criteria for fibrositis	
details	*Inclusion criteria:* Met diagnostic criteria for fibrositis. *Exclusion criteria:* Not specified.		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Fibromyalgia				
Study ID	**Fisher 1988**				
Intervention #1	Not reported	Non-individualised	Treatment was an active preparation of R toxicodendron 6c (Boiron). Dosage was two tablets sucked three times daily for one mth.		
Intervention #2	--	--	--		
Comparator #1 (control)	Not reported	Placebo	Clinical metrologist dispensed lactose tablets with 2% pharmaceutical ethanol.		
Comparator #2 (other)	--	--	--		
Comparator #3 (other)	--	--	--		
Co-interventions	None reported				
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Placebo
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Fibromyalgia symptoms	Baseline, end of treatment (1 mth), after crossover (2 mths)	Number of tender spots	Range not specified Higher is worse
2	Primary	Pain	Baseline, end of treatment (1 mth), after crossover (2 mths)	Visual analogue score (VAS)	Study transformed VAS into nominal variables (better or worse than baseline) i.e. higher is better
3	Primary	Sleep	Baseline, end of treatment (1 mth), after crossover (2 mths)	Visual analogue score (VAS)	Transformed VAS into nominal variables (number of participants better or worse than baseline) i.e. higher is better
4	Not specified	Overall assessment	Baseline, end of treatment (1 mth), after crossover (2 mths)	Visual analogue score (VAS)	Transformed VAS into nominal variables (number of participants better or worse than baseline) i.e. higher is better
5	--	--	--	--	--
6	--	--	--	--	--

Characteristics of included studies	Fibromyalgia				
Study ID	**Fisher 1988**				
7	--	--	--	--	--
8	--	--	--	--	--
9	--	--	--	--	--
7	--	--	--	--	--
8	--	--	--	--	--
9	--	--	--	--	--
10	--	--	--	--	--
11	--	--	--	--	--
12	--	--	--	--	--
Method of analysis					
Statistics	Method of statistical analysis not specified				
Population analysed	Intent-to-treat	Presumed ITT. Number analysed not reported			
Missing data	Not specified	Missing data not reported			

Characteristics of included studies	Fibromyalgia		
Study ID	**Relton 2009**		
Study reference	Relton C, Smith C, Raw J, Walters C, Adebajo AO, Thomas KJ, et al. Healthcare provided by a homeopath as an adjunct to usual care for Fibromyalgia (FMS): results of a pilot Randomised Controlled Trial. Homeopathy: the Journal of the Faculty of Homeopathy. 2009;98(2):77-82. EUCTR2005-004511-29-GB; ISRCTN74040048		
Study design	RCT		Independent statistician performed randomisation using SPSS random number generator and block randomisation. Patients received allocation in opaque sealed envelope
Author affiliation	Authors affiliated with universities and a hospital in the UK		
Source of funds	Funded by Barnsley Hospital NHS Foundation Trust and the charity Homeopathy Action Trust. CR was supported by the DH-National Co-ordinating Centre for Research Capacity Development.		
Declared interests of study authors	The authors declared no conflict of interest		
Setting / provider	Community		
Country(s) / region	UK		
Enrolment period	Not reported		
Length of intervention & follow up	Intervention consisted of up to four interviews (4-6 wks apart). Outcomes measured after 22 wks		
Description of population	*N=*	*Description*	
participants	47	Adults with diagnosed primary FMS	
details	*Inclusion criteria:* Adults with a diagnosis of primary FMS (according to ACR criteria) *Exclusion criteria:* Pain from traumatic injury or structural disease, rheumatoid arthritis, inflammatory arthritis, autoimmune diseases, immunosuppressant treatment, oral steroid treatment, acupuncture treatment, homeopathic treatment, substance abuse, primary psychiatric diagnosis or illness, chronic sedative use, pregnancy or lactation.		
Description of intervention/ comparator	*n=*	Type of intervention	*Description (include treatment duration, remedy chosen, oral vs topical, potency and dosage).*

Characteristics of included studies	Fibromyalgia				
Study ID	**Relton 2009**				
Intervention #1	23	Individualised	Participants completed an initial one hour in depth interview followed by up to four 30min in depth interviews (4-6 wks apart) with individually tailored homeopathic medicines prescribed at each interview.		
Intervention #2	--	--	--		
Comparator #1 (control)	24	Inactive control	Control (no intervention)		
Comparator #2 (other)	--	--	--		
Comparator #3 (other)	--	--	--		
Co-interventions	Usual care - both intervention and control groups received usual care (physiotherapy, aerobic exercise, analgesics, non-steroidal anti-inflammatory drugs or anti-depressants)				
Is comparator clearly inactive?	Yes	Comparison= included in evidence synthesis			Control (no intervention)
Outcomes (measure, description, tool, timing)	*Primary?*	*Description*	*timing*	*measured with*	*measure details*
1	Primary	Fibromyalgia impact	Baseline, interim (12 wks), end of treatment (22 wks)	Fibromyalgia impact questionnaire (FIQ)	Range: 0-100 Higher is worse
2	Secondary	Pain	Baseline, interim (12 wks), end of treatment (22 wks)	Fibromyalgia impact questionnaire (FIQ)	Range: 0-10 Higher is worse
3	Secondary	Fatigue	Baseline, interim (12 wks), end of treatment (22 wks)	Fibromyalgia impact questionnaire (FIQ)	Range: 0-10 Higher is worse
4	Secondary	Tiredness	Baseline, interim (12 wks), end of treatment (22 wks)	Fibromyalgia impact questionnaire (FIQ)	Range: 0-10 Higher is worse
5	Secondary	Stiffness	Baseline, interim (12 wks), end of treatment (22 wks)	Fibromyalgia impact questionnaire (FIQ)	Range: 0-10 Higher is worse
6	Secondary	Number of days felt good	Baseline, interim (12 wks), end of treatment (22 wks)	Fibromyalgia impact questionnaire (FIQ)	Range 0-10 Higher is better

Characteristics of included studies	Fibromyalgia					
Study ID	**Relton 2009**					
7	Secondary	Sensory Pain	Baseline, interim (12 wks), end of treatment (22 wks)	McGill pain questionnaire	Range: 0-33 Higher is worse	
8	Secondary	Affective pain	Baseline, interim (12 wks), end of treatment (22 wks)	McGill pain questionnaire	Range: 0-12 Higher is worse	
9	Secondary	Sensory and Affective pain	Baseline, interim (12 wks), end of treatment (22 wks)	McGill pain questionnaire	Range: 0-45 Higher is worse	
7	Secondary	Fibromyalgia symptoms	Baseline, interim (12 wks), end of treatment (22 wks)	Measure your medical outcomes (MYMOP)	Range: 0-6 Higher is worse	
8	Secondary	Quality of life	Baseline, interim (12 wks), end of treatment (22 wks)	EQ-5D quality of life score	Range: -0.5 - 1.0 Higher is better	
9	Secondary	Anxiety and depression	Baseline, interim (12 wks), end of treatment (22 wks)	Hospital anxiety and depression scale (HADS)	Range: 0-42 Higher is worse	
10	Secondary	Fibromyalgia symptoms	Baseline, interim (12 wks), end of treatment (22 wks)	Tender point count	Range: 0-18 Higher is worse	
11	Not specified	Pain	Baseline, interim (12 wks), end of treatment (22 wks)	Visual analogue score	Range: 0-100 Higher is worse	
12	--	--	--	--	--	--
Method of analysis						
Statistics	Analysis looked for differences between treatment groups at baseline and 22 wks, adjusted for baseline scores by analysis of covariance (ANCOVA). Group scores at 22 wks compared using unpaired t-tests and ANCOVA to adjust for baseline scores and treatment group using complete case analysis scores. Change from baseline assessed using one sided t-test and comparison to zero for each group.					
Population analysed	Intent-to-treat	ITT specified and conducted.				
Missing data	Yes	11/47 participants withdraw from the study. Used last value carried forward to estimate the missing values.				