Table 1: Classification criteria for levels of evidence

Levels of evidence	Criteria
A (Strong Scientific Evidence)	Statistically significant evidence of benefit from >2 properly randomized trials (RCTs), OR evidence from one properly conducted RCT AND one properly conducted meta-analysis.
B (Good Scientific Evidence)	Statistically significant evidence of benefit from 1-2 properly randomized trials, OR evidence of benefit from >1 properly conducted meta-analysis OR evidence of benefit from >1 cohort/case-control/non-randomized trials.
C (Unclear or conflicting scientific evidence)	Evidence of benefit from >1 small RCT(s) without adequate size, power, statistical significance, or quality of design by objective criteria, OR conflicting evidence from multiple RCTs without a clear majority of the properly conducted trials showing evidence of benefit or ineffectiveness.
D (Fair Negative Scientific Evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from cohort/case control/ non-randomized trials.
E (Strong Negative Scientific Evidence)	Statistically significant negative evidence (i.e. lack of evidence of benefit) from >1 properly randomized adequately powered trial(s) of high-quality design by objective criteria.
Lack of Evidence	Unable to evaluate efficacy due to lack of adequate available data. This is not equivalent to negative evidence.

Table 2: Classification of clinical studies

Level of evidence	Study design
1a	Double-blind randomized clinical trials
1b	Non-blinded randomized clinical trials, including those comparing homeopathy with conventional therapy as control (equivalence studies)
2	Non-randomized controlled clinical trials, including those comparing homeopathy with conventional therapy (equivalence studies)
3	Prospective observational studies, without control group
4	Retrospective studies of case-series

Table 3: Classification of publications according to type

Class	Publication type
1a	Mainstream medicine indexed , peer-reviewed, journal
1b	Complementary/alternative medicine indexed, peer reviewed, journal
2	Non-indexed journal
3	Book or book chapter, conference proceedings

Table 4: Details of controlled trials on bronchial asthma

References	Study and publication type	Aim	Population and setting	Inclusion and exclusion criteria	Design	Intervention	Control	No. of patients – attrition – ITT/PP	Key results	Funding – conflict of interest
Campbell JH, et al, 1990 [26]	1a-1a	Efficacy of HIT	Adults; US	Not detailed	Double blind, randomized, parallel arm, placebo controlled	Usual care plus allergen 30c (n=14)	Usual care plus placebo (n=14)	28–?–?	Less intensity (VAS) of symptoms in verum than placebo – significant difference of 93.3 mm; no difference in spirometry	Not stated
Boucinhas JC, et al, 1990 [27]	2-2	Efficacy of Lung histamine C5	Children; France	History of at least 3 asthmatic crises	Open, non-randomized, controlled	Non-individualized standardized Lung histamine C5 (n=109)	No treatment (n=26)	135-14.1%-PP (n=116)	Decrease in number of asthmatic crises in verum (0.38±0.59 vs. 1.54±1.01)	Not stated
Reilly D, et al, 1994 [28]	1a-1a	Efficacy of additive HIT to conventional care	Adults; Asthma specialist outpatient clinic in Scotland	Allergic asthma, mostly sensitivity to house-dust mite, >15% improvement of FEV1 with bronchodilators, >1 year history, atopy (reactive to inhaled allergens and positive skin tests), age >16 years	Double blind randomized parallel arm placebo controlled Schedule: 4 weeks placebo run-in pre-randomization qualification period, 4 weeks treatment, 4 weeks optional follow-up	Lactose or sucrose globules impregnated with individual allergens in potency C30; 3 doses of globules within 24 hours (once).	Lactose or sucrose globules impregnated with diluents only; 3 doses of globules within 24 hours (once)	28-14.3%-PP (n=24)	Significant difference found for severity of symptoms (VAS); it decreased 7.2±3.2 mm in verum but increased 7.8±3.0 mm in placebo (P=0.003); similar trend in lung function and bronchial reactivity; drop-outs or withdrawals: 2 in each group	Not stated
Freitas LAS, et al., 1995 [29]	1a-1b	Efficacy of Blatta orientalis C6 in pediatric asthma	Children; Homeopathy outpatient clinic in Sao Paulo,	At least 3 bronchospastic episodes with intervals of 3 months or less,	Double blind, randomized, parallel group,	Non-individualized, standardized Blatta orientalis C6, 2 globules 3	Indistinguishable placebo, 2 globules 3 times per day for 6 months	86-19.8%-PP (n=69)	M 34, F 35; age range 1-12 yrs; no significant difference in score combining frequency (severity 7.55±7.83 in	Not stated

			Brazil	or continuous wheeze for at least 3 months	placebo-controlled	times per day for 6 months			verum and 9.02±8.63 in placebo), duration and intensity of bronchospastic episodes	
Matusiewicz R, et al., 1995 [30]	1a-2	Efficacy of additive Engystol N® to usual care	Adults; Polish Hospital	Corticosteroid-dependent bronchial asthma, confirmed by history and spirometry; treated with Triamcinolone 4-8 mg daily for at least 5 yrs	Double blind, randomized, parallel group, placebo controlled	1 ampoule Engystol N® (complex homeopathic remedy consisting of Vincetoxin D6/D10/D30, Sulfur D4/D10) , injected subcutaneously at intervals of 5 to 7 days; plus methylxanthines for mucolysis and tetracycline for exacerbations	1 ampoule placebo in addition to mentioned usual care	50 (unclear if this number refers to number of patients randomized , analysed or completing the study)- ?-?	Insufficient reporting, 'clear difference' reported in lung function, medication use, granulocyte function; drop-outs/ withdrawals not reported; mean PEFR change – verum: from 200 to 330 ml; placebo: from 210 to 190 ml	Not stated
Matusiewicz R, 1996 [31]	1a-2	Efficacy of Traumeel S®	Adults; Polish Hospital	Corticosteroid-dependent bronchial asthma, confirmed by history and spirometry; treated with Triamcinolone 4-8 mg daily for at least 5 yrs	Double blind, non-randomized, parallel group, placebo controlled	Weekly subcutaneous injection of Traumeel S® (a combination of 14 homeopathic remedies) or placebo for 20 weeks	Weekly subcutaneous injection of placebo for 20 weeks	103 (unclear if this number refers to number of patients randomized , analysed or completing the study)- ?-?	No difference between groups for lung function but lower use of corticosteroids in the treatment group; mean PEFR levels were 302 ml in verum and 290 ml in placebo	Not stated
Lara-Marquez ML, et al, 1997 [32]	1a-3	Efficacy of individualized homeopathy	Adults; Venezuela	Not detailed	Double blind, randomized, parallel arm, placebo controlled	Individualized homeopathy	Placebo	19 (unclear if this number refers to number of patients randomized , analysed or	Verum better than placebo symptomatically; significant changes in spirometry and immunological markers	Not stated

								completing the study)-?-?		
Jansen GRHJ, et al, 1997 [33]	1a-3	Efficacy of additive individualized homeopathy to standard care	Adults; the Netherlands	Inclusion: Age between 6-17 or 18-55 yrs, ≥15/70 points on 7-item asthma severity scale, written consent; Exclusion: homeopathic treatment with ≥ 30C within 2 months, disorders similar to asthma, severe concomitant disorders, systemic immune-suppressive within 6 months	Double blind, randomized, parallel arm, placebo controlled in the context of usual care; 3 weeks baseline, followed by 3 medication cycles of 7 weeks each	Individualized homeopathy; potency 200C (standardized)	Placebo	58 (stage I and II) and 11 (stage III)-?-?	Study was ongoing – stages I-III completed, stage IV to be initiated; results not disclosed. Outcome measures chosen were changes in severity of asthmatic complaints, peak flow, consumption of anti-asthmatic drugs, and general well being	Not stated
Riveron-Garrote M, et al, 1998 [34]	1a-2	Efficacy of individualized homeopathy	Adults; Mexico	Not detailed	Double blind, randomized, parallel arm, placebo controlled	Individualized homeopathy	Placebo	63 (unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	Number of asthma attacks (4 m) was less in verum than in control ($p<0.05$)	Not stated
Matusiewicz R, et al., 1999 [35]	1a-2	Efficacy of additive	Adults; Polish	Chronic bronchial	Double blind,	1 ampoule of Asthma H® (a	1 ampoule of placebo	84 (unclear if this	Insufficient reporting; significant effect in	Not stated

		Asthma H® to usual care	Hospital	asthma based on history, spirometry, physical examination and medication use; severity unclear; Triamcinolone use 4-8 mg daily for at least 5 yrs	randomized, parallel arm, placebo controlled	complex remedy consisting of 14 homeopathic potencies of D3, D4, D5 and D6) injected subcutaneously at intervals of 5 to 7 days	injected subcutaneously at intervals of 5 to 7 days	number refers to number of patients randomized, analysed or completing the study) plus 20 healthy controls-?-?	reduction of medication use, immune functioning, global rating and number of infections	
Lewith G, et al, 2002 [36]	1a-1a	Efficacy of house dust mite 30c	Adults; 38 general practices in Hampshire and Dorset	Inclusion: mild to severe asthma; 15% improvement in lung function after bronchodilator, plus at least two of the following: asthma symptom diary score>1; variation in PEF>15% on at least 7/14 baseline days; inhaled Salbutamol on at least 7/14 baseline days; positive skin prick test to house dust mite with response greater than aeroallergens	Double blind, randomized, parallel arm, placebo controlled. Study schedule: 4 weeks run-in, 1 day treatment, 16 weeks follow-up	HIT house dust mite 30C; 3 doses orally in 24 hours	Indistinguishable placebo; 3 doses orally in 24 hours	242-16.5%-PP (n=202).	Mean age: verum 38.2, placebo 37.9; no difference found in lung function, medication use, subjective symptoms; drop-outs/ withdrawals: verum 21, control 19. Mean FEV1 improvement was 0.14 l/sec in verum and 0.41 l/sec in placebo. Significant interactions reported between treatment group and week of assessment. No adverse events reported.	Funding from Smith's Charity, NHS Executive South and West Research and Development Directorate, Boiron, and Maurice Laing Foundation; conflict of interest none stated.

				tested. Exclusion: no impairment in QoL during 14 day run-in period; non-completion of study diary >4/14 days; recent participation in another drug trial (<30 days); any previous homeopathic prescribing; pregnancy or lactation; RTI <3 weeks; suspicion of poor compliance; change in concurrent medication<2 weeks					
Suri JC, et al, 2002 [37]	1a-2	Efficacy of Spenglersan Kolloid K®	Adults; Germany	Not detailed	Double blind, randomized, parallel arm, placebo controlled	Homeopathy complex: Spenglersan Kolloid K® consisting of antigens and antitoxins from Staphylococcus aureus subsp., Aureus D9; Streptococcus pneuminae subsp. Pneuminae Dil. D9	Placebo	66 (unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	Patients rated symptom improvement in 23/33 homeopathy patients and 8/33 placebo patients	Funding: Spenglersan GmbH, Germany

White A, et al, 2003 [38]	1a-1a	Efficacy of additive individualized homeopathy to usual care	Children; primary care (3 non-medically qualified homeopaths' practices), UK	Inclusion: GPs diagnosis and prescription for either β-agonist or corticosteroid inhaler in previous 3 months. Exclusion: oral corticosteroids in last 12 months, previous consultation with homeopath, suspicion of poor compliance	Double blind, randomized, parallel arm, placebo controlled	Any number of individualised homeopathy prescriptions. Up to 6 consultations (plus telephone consultations if required) throughout the year. Use of adjunctive therapies allowed by practitioner	Placebo with adjunctive therapies	93-16.1%-PP (n=78)	Age 5-15 years; 46% female. Comparable baseline characteristics. No significant difference in lung function at 52 weeks and quality of life; starting lung function not much different from healthy individuals (PEF 100.4 and 96.9% pred.); so unclear how much change could occur and doubt over whether the quality of life measure was sensitive enough to change. 13 adverse events (none serious) reported in verum and 10 in placebo	The Prince of Wales's Foundation for Integrated Health, London; Ainsworth's Pharmacy, London; Glaxo SmithKline; conflict of interest: none stated.
Delzoppo G, 2004 [39]	1b-2	Efficacy of anti-homotoxic therapy in asthma	Adults; Italy	Not detailed	Open, randomized, parallel arm, active controlled (equivalence trial)	Antihomotoxic therapy: Arnica heel®; Drosera-Homaccord®; Tartephedreel®; Cuprum-Heel®; Belladonna-Homaccord®	Conventional therapeutic strategy (e.g. Beclomethasone)	30 (unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	Comparable results in both groups	Funding: Heel
Mayra RG, etal, 2005 [40]	2-2	Effectiveness of a homeopathic complex Biomodulin T	Infants; Cuba	83 infants with recurrent respiratory infections, 51 males and 32 females; no further details	Cross-sectional, randomized epidemiolog-ical study; 3 parallel arms – A (Biomodulin T; n=28), B	Biomodulin T®	Usual care	83 (unclear if this number refers to number of patients randomized, analysed or	Complete leukogram, global eosinophil count and thymic ultrasound showed better values for groups A and B, not in children belonging to group C	Not stated

					(Biomodulin T plus IH; n=28), and C (std. therapy)			completing the study)- ?-?		
Thompson EA, et al, 2011 [41]	1b-1b	Efficacy of additive individualized homeopathy to standard care	Children; Bristol Royal Hospital for Children (BRHC) and Southmead Hospital (SMH), Bristol, UK	Inclusion: children aged 7-14 years, seen in a secondary care respiratory clinic Exclusion: children who were presently using homeopathy, who were too unwell to take part or refused informed consent	Single blind, (quasi) randomised, parallel arm, active controlled	Individualized homeopathy plus standard treatment	Standard treatment	39-10.3%- PP (n=35)	Poor asthma control in both groups; no additional benefit either medically or financially	Avon Primary Care Research Collaborative; conflict of interest: none stated

'?': Data not available

Table 5: Details of excluded non-controlled trials on bronchial asthma

References	Study and publication type	Aim	Population and setting	Inclusion and exclusion criteria	Design	Intervention	No. of patients – attrition – ITT/PP	Key results	Funding – conflict of interest
Anil RB, et al, 1982 [42]	3, 2	Role of Arseniucm iodatum in acute asthma	Adults; CCRH Unit, Bombay, India	Not detailed	Open, observational, non-randomized, uncontrolled	Homeopathic Arsenicum iodatum and Tuberculinum in different strategies	115 (unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	Significant improvement 82.6%, moderate 8.7%, mild 8.7%	Study funded by CCRH; conflict of interest: none stated
Anil RB, et al, 1988 [43]	3, 2	Role of specific medicines in asthma	Adults; CCRH Unit, Bombay, India	Not detailed	Open, observational, non-randomized, uncontrolled	Homeopathic Arsenicum album and iodatum (N=96), Kali carbonicum (N=60), and Natrum sulphuricum (N=51) in different strategies	207 (unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	No details; symptomatology of prescribed medicines were verified, proving symptoms added	Study funded by CCRH; conflict of interest: none stated
Sachdeva OP, et al, 1988 [44]	3, 2	Role of Arseniucm album in asthma	Adults; CCRH Unit, Bombay, India	Not detailed	Open, observational, non-randomized, uncontrolled	Homeopathic Arsenicum album in different potencies	106 (unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	Significant improvement in long standing cases; verified symptoms enlisted	Study funded by CCRH; conflict of interest: none stated
Mosquera PMF, 1990 [45]	4, 3	Role of individualized homeopathy in pediatric asthma	Children; Mexico	Not detailed	Open, observational, non-randomized, uncontrolled	Individualized homeopathic medicines in different potencies	120 (unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	Improvement in general assessment in most cases	Not stated
Castellsagu API, 1992 [46]	4, 1b	Role of individualized homeopathy in asthma	Adults (n=12) and children (n=14); Italy	Not detailed	Open, observational, non-randomized, uncontrolled	Individualized homeopathic medicines in different potencies	26 (unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	Improvement in global evaluation in most (57%) patients	Not stated
Singh H, 1992 [47]	3, 2	Role of individualized homeopathy in asthma	Adults; CCRH unit, New Delhi	Not detailed	Open, observational, non-randomized, uncontrolled	Individualized homeopathic medicines in different potencies	413 (extrinsic asthma 273, intrinsic asthma 140; unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	Improvement in majority of cases; further details not available	Study funded by CCRH; conflict of interest
Eizayaga and	4, 1b	Role of	Adults;	Inclusion:	Retrospective	Individualized	62 (M 37, F25; age	Significant	Not stated

Eizayaga, 1996 [48]		individualized homeopathy in asthma	Private clinic, Argentina	typical regular asthmatic attacks, illness persisting for one year or longer, at least 8 months of homeopathic treatment Exclusion: other diseases causing pulmonary obstruction, associated pathologies (heart disease, TB etc.)	, non-randomized, uncontrolled	homeopathic medicines in different potencies	19.5±14.2 yrs; unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	decrease of symptom score	
Sharma SR, 1999 [49]	3, 2	Role of individualized homeopathy in asthma	Adults; CCRH unit, Shimla	Not detailed	Open, observational, non-randomized, uncontrolled	Individualized homeopathic medicines in different potencies	331 (unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	Improvement in 294 patients	Study funded by CCRH; conflict of interest: none stated
Li AM, et al, 2003 [50]	3, 1a	Role of additive HIT in asthma	Children; Prince of Wales Hospital, Hong Kong	Stable asthma with no clinical indication for change in treatment, on any dose of inhaled corticosteroid and any other asthma medications; raised eNO level at the start of the study despite clinical stability;	Open, observational, non-randomized, uncontrolled	Additive HIT prepared from individual allergens – house dust mite, cat dander, or both	12 (4 boys, median age 13.5 years, range 7–18; unclear if this number refers to number of patients randomized, analysed or completing the study)-?-?	No improvement in spirometry	Not stated

	identifiable sensitivity to house dust mite or cat and HDM by history and skin prick test; no hospital admission or emergency department attendance for asthma in the previous 3 months; no history of consumption of oral corticosteroid in the previous 3 months; no homeopathic treatment within the previous 6 months, allergen desensitization within the previous year, or HDM avoidance measures or removal of household pet to which the subject had a positive SPT in the previous 3 months	

Vichitra AK, et al, 2008 [51]	3, 2	Role of individualized homeopathy in asthma	Adults; 5 CCRH units, India	Not detailed	Open, observational, non-randomized, uncontrolled	Individualized constitutional homeopathic medicines in different potencies	2461-14.4%-PP (n=2107)	Cured: 52; improvement marked 856, moderate 444, mild 522; no improvement 233; 5 groups of remedies identified for varied purposes	Study funded by CCRH; conflict of interest: none stated
Pinto S, 2012 [52]	3, 2	Role of individualized homeopathy in asthma	Adults; India	Not detailed	Open, observational, non-randomized, uncontrolled	Individualized homeopathic medicines in different potencies	41-43.9%-PP (n=23)	Relevant laboratory parameters improved significantly ($p<0.01$)	Not stated
Shafei HF, 2012 [53]	3, 1b	Role of additive individualized homeopathy to conventional care in asthma	Children aged 7-15 yrs; Homeopathic Clinic, National Research Centre, Cairo, Egypt	Exclusion: Children who had previously consulted a homeopath and received a homeopathic prescription, children unable to complete the necessary follow-up period or were suffering from systemic disease or congenital anomalies	Open, observational, longitudinal, non-randomized, uncontrolled	Individualized homeopathic medicines in different potencies	42-28.6%-PP (n=30)	Significant improvement in frequency and severity of attacks, use of medication, night awakening and spirometry after 3 and 6 months	Not stated

'?': Data not available

Table 6: Methodological quality analysis of the included trials by Jadad scoring

Ref.	Randomization	Blinding	Withdrawal or drop-outs	Total
Campbell JH, et al, 1990 [26]	2	2	0	4
Boucinhas JC, et al, 1990 [27]	0	0	1	1
Reilly D, et al, 1994 [28]	1	2	1	4
Freitas LAS, et al., 1995 [29]	1	2	1	4
Matusiewicz R, et al., 1995 [30]	0	1	0	1
Matusiewicz R, 1996 [31]	0	1	0	1
Lara-Marquez ML, et al, 1997 [32]	1	1	0	2
Jansen G, et al, 1997 [33]	1	1	0	2
Riveron-Garrote M, et al, 1998 [34]	1	1	0	2
Matusiewicz R, et al, 1999 [35]	1	1	0	2
Lewith G, et al, 2002 [36]	2	2	1	5
Suri JC, et al, 2002 [37]	1	1	0	2
White A, et al, 2003 [38]	2	2	1	5
Delzoppo G, 2004 [39]	2	0	0	2
Mayra RG, et al, 2005 [40]	1	0	0	1
Thompson EA, et al, 2011 [41]	1	1	1	3

Table 7: Risk of bias analysis of the included trials by Cochrane Collaboration Tool

References	Domain I: Random sequence generation	Domain II: Allocation concealment	Domain III: Blinding of participants and personnel	Domain IV: Blinding of outcome assessors	Domain V: Incomplete outcome data	Domain VI: Selective reporting	Domain VII: Anything else	Overall RoB	RoB rating
Campbell JH, et al, 1990 [26]	Y	Y	Y	U	U	U	U	Uncertain	B4
Boucinhas JC, et al, 1990 [27]	N	N	N	N	N	U	U	High	C5.2
Reilly D, et al, 1994 [28]	Y	Y	Y	Y	N	U	U	High	C1.2
Freitas LAS, et al., 1995 [29]	Y	Y	Y	Y	N	U	U	High	C1.2
Matusiewicz R, et al., 1995 [30]	Y	U	Y	Y	U	U	U	Uncertain	B4
Matusiewicz R, 1996 [31]	N	U	Y	U	U	U	U	High	C1.5
Lara-Marquez ML, et al, 1997 [32]	Y	Y	Y	U	U	U	U	Uncertain	B4
Jansen G, et al, 1997 [33]	Y	U	Y	U	U	U	U	Uncertain	B5
Riveron-Garrote M, et al, 1998 [34]	Y	Y	Y	U	Y	U	U	Uncertain	B3
Matusiewicz R, et al, 1999 [35]	U	U	Y	Y	U	U	U	Uncertain	B5
Lewith G, et al, 2002 [36]	Y	Y	Y	Y	N	U	U	High	C1.2
Suri JC, et al, 2002 [37]	Y	Y	Y	U	U	U	U	Uncertain	B4
White A, et al, 2003 [38]	Y	Y	Y	Y	N	U	U	High	C1.2
Delzoppo G, 2004 [39]	Y	N	N	N	U	U	U	High	C3.3
Mayra RG, et al, 2005 [40]	Y	U	U	U	U	U	U	Uncertain	B6
Thompson EA, et al, 2011 [41]	Y	U	Y	N	N	U	U	High	C2.3

Y: Yes; N: No; U: Uncertain

Table 8: Model validity assessment of the included trials by Mathie's criteria

References	Domain I: Rationale for the choice of the particular homeopathic intervention	Domain II: Homeopathic principles reflected in the intervention	Domain III: Extent of homeopathic practitioner input	Domain IV: Nature of the main outcome measure	Domain V: Capability of the main outcome measure to detect change	Domain VI: Length of the follow-up to the endpoint of the study	Overall validity	Validity rating
Campbell JH, et al, 1990 [26]	U	N	N	Y	Y	Y	Inadequate	C2.1
Boucinhas JC, et al, 1990 [27]	U	N	N	U	U	Y	Inadequate	C2.3
Reilly D, et al, 1994 [28]	U	N	N	Y	Y	Y	Inadequate	C2.1
Freitas LAS, et al., 1995 [29]	U	N	N	U	U	Y	Inadequate	C2.3
Matusiewicz R, et al., 1995 [30]	U	N	N	Y	Y	Y	Inadequate	C2.1
Matusiewicz R, 1996 [31]	U	N	N	Y	Y	Y	Inadequate	C2.1
Lara-Marquez ML, et al, 1997 [32]	Y	Y	U	Y	Y	Y	Acceptable	B1
Jansen G, et al, 1997 [33]	Y	U	Y	Y	Y	Y	Acceptable	B1
Riveron-Garrote M, et al, 1998 [34]	Y	Y	U	U	U	Y	Uncertain	B3
Matusiewicz R, et al, 1999 [35]	U	N	N	U	U	Y	Inadequate	C2.3
Lewith G, et al, 2002 [36]	U	N	N	Y	Y	Y	Inadequate	C2.1
Suri JC, et al, 2002 [37]	U	N	N	U	U	Y	Inadequate	C2.3
White A, et al, 2003 [38]	Y	Y	Y	Y	Y	Y	Acceptable	B1
Delzoppo G, 2004 [39]	U	N	N	U	U	U	Inadequate	C2.4
Mayra RG, et al, 2005 [40]	U	N	N	Y	Y	Y	Inadequate	C2.1
Thompson EA, et al, 2011 [41]	Y	Y	Y	U	U	Y	Uncertain	B3

Y: Yes; N: No; U: Uncertain

Table 9: Quality of individualization assessment of the included trials by Saha's criteria

References	Criterion I: Single medicine prescription when required on each occasion	Criterion II: Medicine individualisation	Criterion III: Proper description of approach to medicine individualisation	Criterion IV: Dose individualisation	Criterion V: Proper description of approach to dose individualisation	Criterion VI: Subsequent prescriptions as per Kent's observations and/or Hering's law	Score
Campbell JH, et al, 1990 [26]	Y	N	N	N	N	N	1
Boucinhas JC, et al, 1990 [27]	Y	N	N	N	N	N	1
Reilly D, et al, 1994 [28]	Y	N	N	N	N	N	1
Freitas LAS, et al., 1995 [29]	Y	N	N	N	N	N	1
Matusiewicz R, et al., 1995 [30]	N	N	N	N	N	N	0
Matusiewicz R, 1996 [31]	N	N	N	N	N	N	0
Lara-Marquez ML, et al, 1997 [32]	Y	Y	U	Y	U	U	3
Jansen G, et al, 1997 [33]	Y	Y	U	N	N	U	2
Riveron-Garrote M, et al, 1998 [34]	Y	Y	U	Y	U	U	3
Matusiewicz R, et al, 1999 [35]	N	N	N	N	N	N	0
Lewith G, et al, 2002 [36]	Y	N	N	N	N	N	1
Suri JC, et al, 2002 [37]	N	N	N	N	N	N	0
White A, et al, 2003 [38]	Y	Y	U	Y	U	U	3
Delzoppo G, 2004 [39]	N	N	N	N	N	N	0
Mayra RG, et al, 2005 [40]	N	N	N	N	N	N	0

Thompson EA, et al, 2011 [41]	Y	Y	U	Y	U	U	3

Y: Yes; N: No; U: Uncertain

Table 10: Risk of bias analysis of the excluded observational studies by Cochrane Collaboration Tool

References	Domain I: Confounding	Domain II: Selection of participants into the study	Domain III: Measurement of interventions	Domain IV: Departures from intended interventions	Domain V: Accounting for missing data	Domain VI: Measurement of outcomes	Domain VII: Selection of reported results	Overall RoB	RoB rating
Anil RB, et al, 1982 [42]	Y	U	U	N	N	N	U	High	C3.3
Anil RB, et al, 1988 [43]	Y	U	U	N	N	N	U	High	C3.3
Sachdeva OP, et al, 1988 [44]	Y	U	U	N	N	N	U	High	C3.3
Mosquera PMF, 1990 [45]	Y	U	Y	N	N	N	U	High	C3.2
Castellsagu API, 1992 [46]	Y	U	Y	N	N	N	U	High	C3.2
Singh H, 1992 [47]	Y	Y	Y	N	N	N	U	High	C3.1
Eizayaga and Eizayaga, 1996 [48]	Y	Y	Y	N	N	N	U	High	C3.1
Sharma SR, 1999 [49]	Y	U	Y	N	N	N	U	High	C3.2
Li AM, et al, 2003 [50]	Y	Y	Y	N	N	Y	U	High	C1.1
Vichitra AK, et al, 2008 [51]	Y	Y	Y	N	N	Y	U	High	C2.1
Pinto S, 2012 [52]	Y	U	Y	N	N	Y	U	High	C2.2
Shafei HF, 2012 [53]	Y	Y	Y	N	N	Y	U	High	C2.1

Y: Yes; N: No; U: Uncertain

Table 11: Model validity assessment of the excluded studies by Mathie's criteria

References	Domain I: Rationale for the choice of the particular homeopathic intervention	Domain II: Homeopathic principles reflected in the intervention	Domain III: Extent of homeopathic practitioner input	Domain IV: Nature of the main outcome measure	Domain V: Capability of the main outcome measure to detect change	Domain VI: Length of the follow-up to the endpoint of the study	Overall validity	Validity rating
Anil RB, et al, 1982 [42]	Y	U	Y	N	N	Y	Inadequate	C2.1
Anil RB, et al, 1988 [43]	Y	U	Y	N	N	Y	Inadequate	C2.1
Sachdeva OP, et al, 1988 [44]	Y	U	Y	N	N	Y	Inadequate	C2.1
Mosquera PMF, 1990 [45]	Y	Y	Y	N	N	Y	Inadequate	C2
Castellsagu API, 1992 [46]	Y	Y	Y	N	N	Y	Inadequate	C2
Singh H, 1992 [47]	Y	Y	Y	N	N	Y	Inadequate	C2
Eizayaga and Eizayaga, 1996 [48]	Y	Y	Y	N	N	Y	Inadequate	C2
Sharma SR, 1999 [49]	Y	Y	Y	N	N	Y	Inadequate	C2
Li AM, et al, 2003 [50]	U	N	N	Y	Y	Y	Inadequate	C2.1
Vichitra AK, et al, 2008 [51]	Y	Y	Y	N	N	Y	Inadequate	C2
Pinto S, 2012 [52]	Y	Y	Y	Y	Y	Y	Acceptable	A
Shafei HF, 2012 [53]	Y	Y	Y	Y	Y	Y	Acceptable	A

Y: Yes; N: No; U: Uncertain

Table 12: Quality of individualization assessment of the excluded trials by Saha's criteria

References	Criterion I: Single medicine prescription when required on each occasion	Criterion II: Medicine individualisation	Criterion III: Proper description of approach to medicine individualisation	Criterion IV: Dose individualisation	Criterion V: Proper description of approach to dose individualisation	Criterion VI: Subsequent prescriptions as per Kent's observations and/or Hering's law	Score
Anil RB, et al, 1982 [42]	Y	U	U	Y	U	U	2
Anil RB, et al, 1988 [43]	Y	U	U	Y	U	U	2
Sachdeva OP, et al, 1988 [44]	Y	U	U	Y	U	U	2
Mosquera PMF, 1990 [45]	Y	Y	Y	Y	U	U	4
Castellsagu API, 1992 [46]	Y	Y	Y	Y	U	U	4
Singh H, 1992 [47]	Y	Y	U	Y	U	U	3
Eizayaga and Eizayaga, 1996 [48]	Y	Y	Y	Y	U	U	4
Sharma SR, 1999 [49]	Y	Y	U	Y	U	U	3
Li AM, et al, 2003 [50]	Y	N	N	N	N	N	1
Vichitra AK, et al, 2008 [51]	Y	Y	Y	Y	U	U	4
Pinto S, 2012 [52]	Y	Y	U	Y	U	U	3
Shafei HF, 2012 [53]	Y	Y	Y	Y	U	U	4

Y: Yes; N: No; U: Uncertain