Review

Veterinary homeopathy: systematic review of medical conditions studied by randomised placebo-controlled trials

Robert T. Mathie, Jürgen Clausen

A systematic review of randomised controlled trials (RCTs) of veterinary homeopathy has not previously been undertaken. Using Cochrane methods, this review aims to assess risk of bias and to quantify the effect size of homeopathic intervention compared with placebo for each eligible peer-reviewed trial. Judgement in seven assessment domains enabled a trial's risk of bias to be designated as low, unclear or high. A trial was judged to comprise reliable evidence if its risk of bias was low or was unclear in specified domains. A trial was considered to be free of vested interest if it was not funded by a homeopathic pharmacy. The 18 eligible RCTs were disparate in nature, representing four species and 11 different medical conditions. Reliable evidence, free from vested interest, was identified in two trials: homeopathic Coli had a prophylactic effect on porcine diarrhoea (odds ratio 3.89, 95 per cent confidence interval [CI], 1.19 to 12.68, P=0.02); and individualised homeopathic treatment did not have a more beneficial effect on bovine mastitis than placebo intervention (standardised mean difference -0.31, 95 per cent CI, -0.97 to 0.34, P=0.35). Mixed findings from the only two placebo-controlled RCTs that had suitably reliable evidence precluded generalisable conclusions about the efficacy of any particular homeopathic medicine or the impact of individualised homeopathic intervention on any given medical condition in animals.

HOMEOPATHY is a system of medicine that uses specific preparations of substances whose effects, when administered to healthy subjects, correspond to the manifestations of the disorder (symptoms, clinical signs, pathological states) in the individual patient. Homeopathic prescribing is thus normally based on the individual's 'totality of symptoms' (Swayne 2000).

In (rightly) extolling the importance of placebo-controlled clinical trial design in evidence-based veterinary medicine, Overall and Dunham (2009) make a key comment about the application of the scientific method in the particular case of homeopathy: 'If homeopathy [wishes] to be considered by scientists, [it] must be shown to be valid using methods that science uses to evaluate all treatment modalities'. This systematic review directly addresses this issue by examining the evidence available in randomised placebo-controlled trials of veterinary homeopathy, using established systematic review methods.

The use of homeopathy in veterinary medicine is highly controversial, with strong viewpoints expressed on each side of the argument (Baker and others 2005, Hektoen 2005). On the one side, homeopathy's proponents point to case reports, non-randomised comparative studies and randomised controlled trials (RCTs) that are perceived to be positive; on the other side, critics highlight the improbable efficacy of very highly diluted medicines, with the conclusion that the research evidence in homeopathy cannot plausibly contain positive findings. Nevertheless, many homeopathic medicines are not in this 'ultra-molecular' range (Rutten and others 2013), and the plausibility argument is being approached directly in new research on nanoparticles (Bell and Schwartz 2013) and other physicochemical properties of dilutions (see Hill and others 2009). Moreover, neither side of the argument has been in a position to know the true and full nature of the clinical research evidence as, until now, no systematic review of RCTs in veterinary homeopathy has been conducted.

A previous systematic search of the published RCTs in veterinary homeopathy by the current authors identified 38 peer-reviewed papers that were regarded as potentially eligible for detailed systematic review (Mathie and others 2012b). Such in-depth reviews can inform the debate surrounding the effectiveness of veterinary homeopathy in general or the efficacy of its medicines for particular medical conditions.

In taking forward the first phase of this in-depth review programme, the approach continued to reflect the above literature analysis, and three principal attributes of research design or intervention were distinguished: (a) controlled by placebo versus controlled by other than placebo; (b) individualised homeopathy versus non-individualised homeopathy; and (c) treatment versus prophylaxis. This review reports findings from an appraisal of placebo-controlled, peer-reviewed trials of veterinary homeopathy (individualised or non-individualised, treatment or prophylaxis).

For each eligible RCT, the aim was to assess the risk of bias (Higgins and Altman 2011), together with the direction, statistical sig-

Veterinary Record (2014) doi: 10.1136/vr.101767

Robert T. Mathie, PhD, British Homeopathic Association, Hahnemann House, 29 Park Street West, Luton LU1 3BE, UK
Jürgen Clausen, PhD, Karl und Veronica Carstens-Stiftung, Am Deimelsberg 36, D-45276 Essen, Germany

E-mail for correspondence: rmathie@britishhomeopathic.org

Provenance: not commissioned; externally peer reviewed

Accepted for publication June 21, 2014

nificance and effect size of homeopathy or placebo on the main outcome measure. For groupings of RCTs per medical condition, we aimed to determine pooled effect size by meta-analysis and, by reflecting study quality critically in our approach, to determine if (and which) homeopathic interventions were more beneficial than placebo, and for which particular medical condition(s). Practical and reporting standards for systematic reviews set by the PRISMA Group (Moher and others 2009) were adhered to throughout.

Methods

Data sources

All randomised and controlled trials that assessed a homeopathic intervention, in any species except people, were eligible for review according to the inclusion/exclusion criteria outlined previously (Mathie and others 2012b).

The following electronic databases were searched, up to and including March 2011 (during peer review, the systematic literature search was updated up to the end of December 2013): AMED, CINAHL, CENTRAL (Cochrane), Embase, Hom-Inform, HomVetCR (Carstens-Stiftung), LILACS, PubMed, Science Citation Index and Scopus. The literature search strategy has been described in detail elsewhere (Mathie and others 2012b).

Identifying papers for full data extraction

Eighteen papers were identified as satisfying the key acceptance criteria: substantive report of clinical treatment or prophylaxis trial in veterinary homeopathic medicine; randomised; controlled by placebo; and published in a peer-reviewed journal (Mathie and others 2012b).

RTM screened and categorised each of the 18 potentially relevant papers to assess their eligibility for full data extraction. JC independently appraised these decisions. Any differences of opinion were resolved by consensus discussion.

Exclusion criteria before data were extracted:

- Research using radionically prepared 'homeopathic' medicines;
- Intervention tested was homeopathy combined with other (complementary or conventional) medicine or therapy.

Fig 1 illustrates the PRISMA flowchart, which focuses solely on previously identified placebo-controlled trials (Mathie and others 2012b). RCTs controlled by a comparator other than placebo are the subject of a separate review. The 18 RCTs included in this systematic review comprised 12 treatment trials and six prophylaxis trials.

Data extraction and management

Because it is recognised that contacting the original authors of trials may lead to overly positive answers (Higgins and Altman 2011), the authors of eligible RCT papers were not approached for clarification on unclear or missing facets of any of their methods or results; however, original authors' references to their previously published study methods were eligible for follow-up and taken into account as appropriate. For each of two assessors working independently, relevant data were extracted and then recorded using a standardised data collection format (Microsoft Excel; Microsoft).

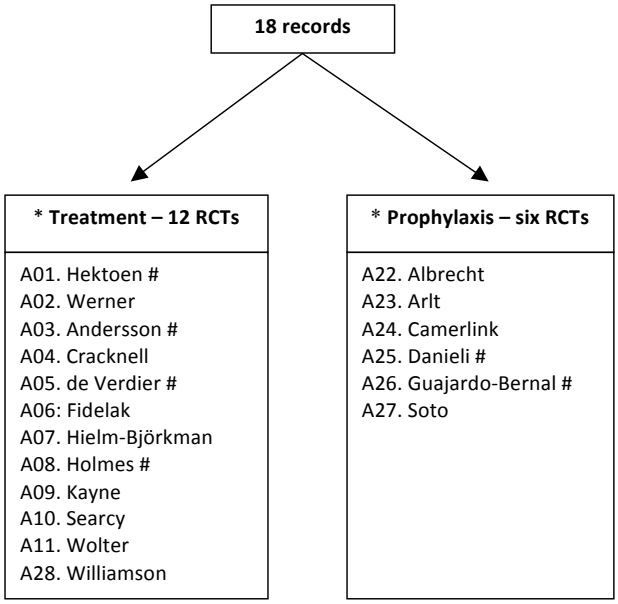

FIG 1: PRISMA flowchart illustrating records of randomised placebo-controlled trials eligible for inclusion in the systematic review

* RCTs are numbered as per a previous paper published by the authors (Mathie and others [2012b]). Publication details of each RCT may be found in the reference list
# Trial with continuous measure as main outcome (unmarked trials have a dichotomous measure as the main outcome)

None of the 18 papers reported more than one RCT. For a paper reporting an RCT that involved more than two groups of subjects, the authors focused data extraction on only one pair of groups as follows: treatment in preference to prophylaxis; and placebo control in preference to other-than-placebo control.

For studies that comprised more than one homeopathy group, the total sample size (and associated outcomes) cited reflected the total number of subjects in the homeopathy groups combined (Higgins and others 2011). This was the approach in all cases, that is, where the same homeopathic medicine was used, and with the same timing of administration, but with different potencies; where the same homeopathic medicine and potency were used, but with different timings of administration; and where a different homeopathic medicine was used.

Assessment of risk of bias

In eligible trials, and using the standard criteria defined by the Cochrane Collaboration (Higgins and Altman 2011), extraction of information enabled appraisal of freedom from risk of bias. There were three options when assessing the trials: 'yes' (low risk of bias), 'unclear' (uncertain risk of bias) or 'no' (high risk of bias).

This approach applied to each of seven assessment domains:

- I – Method used to generate the random sequence;
- II – Method of allocation concealment used to implement the random sequence;
- IIIA – Blinding of trial personnel, including animal owner as appropriate;
- IIIB – Blinding of outcome assessors;
- IV – Whether all randomised patients were completely accounted for in the analysis;
- V – Evidence of selective outcome reporting;
- VI – Evidence of other bias, such as extreme data imbalance at baseline.

For the domain relating to whether all randomised patients were accounted for in the analysis, unless there was indication to the contrary, a trial was regarded as being at high risk of bias if there was greater than 20 per cent participant attrition rate, and irrespective of whether intention-to-treat analysis had been carried out on the data.

For the domain relating to evidence of selective outcome reporting, judgement was based on reported outcomes and not on a comparison with an original trial protocol (as none exists in the public domain for RCTs of veterinary homeopathy) but rather on a comparison with the details given in the materials and methods section in the original paper.

The two assessors' judgements were mutually scrutinised and compared, with discrepancies between them resolved by consensus discussion, with the aim of producing summary of findings tabulations to characterise all eligible trials.

Using the Cochrane approach, each trial was designated as one of the following: at low risk of bias (free of bias in all seven standard domains of assessment); at uncertain risk of bias (unclear judgement of bias for one or more domains, and no evident risk of bias in any

domain); or at high risk of bias (evident risk of bias for one or more domain) (Higgins and Altman 2011).

For each trial that was not found to be at high risk of bias (that is, it did not attain a 'no' response for any domain), the evidence was seen as reliable if it was assessed to be free of bias in each of four domains: randomisation; blinding of trial personnel; blinding of outcome assessors; and patients accounted for in analysis. These criteria for 'reliable evidence' are analogous to those used by Shang and others (2005) in their designation of 'trials of higher methodological quality'. According to these criteria, the latter group included adequacy of allocation concealment (domain II) but excluded completeness of data analysis (equivalent to domain IV). In the veterinary trial context, domain IV was regarded in this study as a more relevant arbiter of reliable evidence than domain II.

For each trial (for the purposes of risk-of-bias assessment and for assessment of treatment effect), the main outcome measure was identified using a refinement of the approaches adopted by Linde and others (1997) and by Shang and others (2005). The main outcome measure of each trial was based on a hierarchical ranking order (consistent with the World Health Organization [WHO 2002] classification system for levels of functioning linked to health condition):

- Mortality;
- Morbidity;
  - Treatment failure;
  - Pathology; symptoms of disease;
- Health impairment (loss/abnormality of function, including apparent presence of pain);
- Limitation of activity (disability, ill health);
- Surrogate outcome (for example, blood test data).

In cases where, according to the judgement of the reviewers, there were two or more outcome measures of equal greatest importance within the above hierarchy, the designated 'main outcome measure' was selected randomly from those two or more options by tossing coins or rolling dice.

The single endpoint (measured from the start of the intervention) associated with the designated main outcome measure was taken as the last follow-up at which data were reported for that outcome. The exceptions to this were two 'semi-crossover' trials (Hektoen and others 2004, Werner and others 2010), for which the single endpoint was taken at seven days after treatment commenced and before any crossover. A semi-crossover study design is one in which patients defined as non-responders after a pre-defined period of time are re-randomised to another arm of the trial.

Summary effect measures for main outcome

For each eligible trial, effect size was taken to be the difference between the homeopathy and the placebo groups at the predetermined endpoint of the trial as follows (Mathie and others 2013):

- For dichotomous measures: odds ratio (OR) with 95 per cent confidence interval (CI);
- For continuous measures: standardised mean difference (SMD), with 95 per cent CI.

For a trial in which the selected dichotomous measure was presented solely as percentage data (tabulated or graphed) per group, the categorical data required for analysis were calculated from the available published information. For a trial in which the selected continuous measure was presented as a mean, but without an associated standard deviation (sd), Cochrane-recognised methods were used to calculate or estimate sd per group (Higgins and Deeks 2011).

If the original paper did not provide adequate information on the designated main outcome measure to enable data extraction, that trial's outcome was classified as 'not estimable' and a further potentially estimable outcome was not sought.

Mean effect size was interpreted as follows: an SMD of less than 0.40 was considered 'small'; an SMD of 0.40 to 0.70 (inclusive) was considered 'moderate'; and an SMD of more than 0.70 was considered 'large' (Schünemann and others 2011). Using the standard formula to convert SMD approximately to OR (Schünemann and others 2011), the corresponding effect size thresholds were calculated as: an OR of less than 2.10 was considered to be 'small'; an OR of 2.10 to 3.60 (inclusive) was considered to be 'moderate'; and an OR of over 3.60 was considered to be 'large'.

Under the separate group headings of individualised homeopathy and non-individualised homeopathy, and for each of any subcategories in which there was more than one RCT paper with extractable data, the authors aimed to determine summary statistics, using meta-analytical methods, for the following:

- Disease-specific prophylactic effects per species;
- Disease-specific treatment effects per species.

All calculations and analyses were performed using Review Manager 5.2 (Cochrane). Given the anticipated heterogeneous data for intervention effects, the random effects (rather than fixed effects) model was planned for each meta-analysis (Deeks and others 2011). For each meta-analysis, the need to merge dichotomous and continuously variable data, using the Cochrane-recognised method, as required, to re-express SMD in terms of OR, was also anticipated (Schünemann and others 2011).

Reflecting overall study quality

The main focus was on the data extracted from trials that were not designated to be at high risk of bias, and especially those that were deemed to contain reliable evidence.

The focus for primary conclusions was trials with reliable evidence that were also not explicitly funded, directly or indirectly, by a homeopathic pharmacy (that is, there was no overt vested interest in the trial's findings).

Direction of effect of treatment/prophylaxis per trial

For a conclusion that homeopathic intervention impacted on health outcome (that is, statistical significance favouring homeopathy, at $P \leq 0.05$), the following were required:

- Dichotomous measure (OR): lower 95 per cent confidence limit of 1 or more;
- Continuous measure (SMD): relevant 95 per cent confidence limit of less than or equal to 0 or more than or equal to 0, depending on the direction of the hypothesis favouring homeopathy.

Results

Demographic details

Table 1 provides details of each of the 18 eligible trials: (i) individualised homeopathy/treatment (two trials); (ii) non-individualised homeopathy/treatment (10 trials); and (iii) non-individualised homeopathy/prophylaxis (six trials). Data presented include: medical condition, species, nature of the homeopathic intervention, and trial setting. The tabulation also includes details of the RCT's source of funding, together with the associated freedom from vested interest: only one trial (Holmes and others 2005) was deemed to be clearly free of such vested interest.

The trials were clinically extremely diverse. In the 18 eligible studies, four different species are represented: cattle (10 trials); dogs (two trials); goats (one trial); and pigs (five trials). Eleven different medical conditions are represented.

Table 2 details sample sizes, designated main outcome measures, and trial endpoints of the included trials. Table 2 also accounts for three trials for which data were not extractable for analysis. Diversity was again apparent, with large variations in sample sizes, main outcome measures and the timing of the trial endpoint.

Risk of bias

Table 3 details risk-of-bias judgements per trial.

Some of the papers were written to such a poor standard that risk-of-bias assessments were not straightforward. However, consensus discussion always resolved the matter. Only one trial had a low risk

TABLE 1: Details of 18 placebo-controlled randomised controlled trials

Condition	Species	Trial	First author	Publication year	Homeopathic medicine	Level of dilution*	Setting	Funding	Free from vested interest	Notes
Individualised homeopathy/treatment										
Mastitis	Cattle	A01	Hektoen	2004	Individualised	Not stated	39 dairy herds in eastern Norway	Government	Unclear	Semi-crossover trial
		A02	Werner	2010	Individualised	Mostly D6 or D12	One organic and three conventional dairy herds in Germany	Government; charity	Unclear	Semi-crossover trial
Non-individualised homeopathy/treatment										
Diarrhoea	Cattle	A05	de Verdier	2003	Podophyllum	D30	12 dairy herds in Sweden	Charity; remedies were gifts from HPC	No	
		A09	Kayne	1994	Arsenicum album	30C	Unstated number of cattle farms in Scotland	Remedies were gifts from HPC	No	
Fear of firework noises	Dogs	A04	Cracknell	2008	Fixed formulation of five remedies	6C, 30C	Dogs whose owners replied to national advertising in the UK	HPC	No	
Induction of farrowing	Pigs	A11	Wolter	1966	Caulophyllum	D30	At least 23 pig herds in Germany	Remedies were gifts from HPC	No	
Infertility	Cattle	A06	Fidelak	2007	Three different complex preparations of over 20 remedies	D1 to D10	One organic dairy herd in Germany	None stated	Unclear	
		A28	Williamson	1995	Sepia (24 to 48 hours and 14 days postpartum)	200C	One dairy herd in Scotland	Remedies were gifts from HPC	No	RCT of homeopathy (group 1) v homeopathy (group 2) v untreated controls v placebo
Mastitis	Cattle	A03	Andersson	1997	Six different remedies	D2 to D12	12 dairy herds in Germany	European Union, remedies were gift from HPC	No	
		A08	Holmes	2005	Mastitis nosode	30C	One dairy herd in England	Charity	Yes	
		A10	Searcy	1995	Complex of three remedies	200C	One dairy herd in Mexico	None stated	Unclear	
Osteoarthritis	Dogs	A07	Hielm-Björkman	2009	Complex of 14 remedies	D2 to D8	Dogs screened via owner-completed telephone interview in Finland	Charities; drug industry; remedies were gifts from HPC	No	RCT of homeopathy v placebo v NSAID
Non-individualised homeopathy/prophylaxis										
Endometritis	Cattle	A23	Arlt	2009	Either two or three different remedies, taken consecutively	Not stated	One dairy herd in Germany	HPC	No	RCT of homeopathy (group 1) v homeopathy (group 2) v placebo
Diarrhoea	Pigs	A24	Camerlink	2010	Coli	30K	One commercial pig farm in the Netherlands	None stated	Unclear	Treated sows and evaluated piglet litters
Growth rate	Pigs	A26	Guajardo-Bernal	1996	Sulphur	201C	One university pig unit in Mexico	None stated	Unclear	
Infectious diseases (respiratory)	Pigs	A22	Albrecht	1999	Complex of five remedies	D1 to D4	One intensive pig farm in Germany	Charity; HPC	No	RCT of homeopathy v placebo v antibiotics
Metabolic disturbance postpartum	Goats	A25	Danieli	2009	Echinacea purpurea	30C	One commercial goat farm in Italy	None stated	Unclear	RCT of homeopathy v placebo v anti-ketogenic v anti-ketogenic+ homeopathy
Reproductive performance	Pigs	A27	Soto	2010	Avena sativa and/or Pulsatilla nigricans	6C	One commercial pig farm in Brazil	None stated	Unclear	RCT of each of three homeopathic remedies v placebo

HPC Homeopathic pharmacy company, RCT Randomised controlled trial.
*Note on homeopathic dilutions: The number refers to the number of successive serial dilutions to which the starting material has been subjected. The letter refers to the scale on which the dilution has been carried out: the letter D denotes the decimal method of dilution (that is, one part of liquid is added to nine parts of purified water, ethanol, glycerol or lactose); the letter C indicates the centesimal method (one part added to 99 parts of diluent). In the Korsakovian method (denoted K), a single piece of glassware is used; this is emptied and refilled, the liquid adhering to the walls of the vessel in which it is diluted. In homeopathic dilutions above 12C/D24 (10^{-24} molar) – beyond Avogadro's constant, 6.02×10^{23} mol^{-1} – there are, in theory, no material traces of the original substance; such dilutions are known as 'ultra-molecular'

TABLE 2: Sample sizes and outcomes

Trial	n start (h)	n start (p)	n start (total)	n end (h)	n end (p)	n end (total)	Attrition (per cent)	Main outcome	Problem with main outcome?	Main outcome used for data extraction	Endpoint	Notes
Individualised homeopathy/treatment												
A01	21	16	37	21	16	37	0.0	Acute mastitis score	No (though sd calculated from 95 per cent CI data, using t-distribution)	Acute mastitis score	Seven days	
A02	58	43	101	58	43	101	0.0	Totally cured quarters	No	Totally cured quarters	Seven days	n=number of udder quarters
Non-individualised homeopathy/treatment												
A05	24	24	48	24	20	44	8.3	Duration of diarrhoea	Yes: sds not given, but common sd calculated from CI data (assuming 95% CI)	Duration of diarrhoea	Up to eight days	
A09	6	10	16	6	9	15	6.3	Animals with 'pasty' stools	No	Animals with 'pasty' stools	48 hours	Authors did not carry out formal statistical analysis of data
A04	35	40	75	34	38	72	4.0	Improved (that is reduced) fear response	No	Improved (that is reduced) fear response	Four weeks	
A11	18	23	41	18	23	41	0.0	Presence of uterine contraction	No	Presence of uterine contraction	20 minutes after treatment	Contractions after birth of first piglet. n=1 excluded from homeopathy group (repeat measurement of placebo group animal)
A06	76	70	146	58	56	114	21.9	Gestating cows	No	Gestating cows	200 days post-partum	
A28	60	30	90	50	26	76	15.6	Held to first service	No (original percentage data used for calculation of odds ratios)	Held to first service	Not stated	n for homeopathy is total for two homeopathically treated groups. It was assumed that a total of 120 cows were randomised to four equal groups
A03	Data not given	Data not given	416	Data not given	Data not given	306	26.4	Bacterial cell counts	Yes, data not given	None usable	37 days	n reflects number of quarters, not number of animals
A08	76	76	152	68	67	135	11.2	Somatic cell counts (only outcome recorded)	Yes, sd not available (logarithmic data)	None usable	28 days	
A10	52	52	104	51	52	103	1.0	Unaffected quarters	No	Unaffected quarters	30 days	n=number of udder quarters. Unaffected quarters identified by CMT
A07	17	17	34	14	15	29	14.7	Improved mobility index	No	Improved mobility index	Eight weeks	Assumes that total n=51 was divided equally into three groups
Non-individualised homeopathy/prophylaxis												
A23	417	200	617	417	200	617	0.0	Absence of endometritis	No	Absence of endometritis	21 to 27 days	
A24	26	26	52	24	26	50	3.8	Absence of diarrhoea	No	Absence of diarrhoea per litter	One week	The sows were treated. n=number of litters
A26	39	40	79	39	40	79	0.0	Piglets' final bodyweight	Yes: sd not given, but common sd calculated from conservative P=0.049	Piglets' final bodyweight	30 days	
A22	480	480	960	480	480	960	0.0	Absence of respiratory tract disease	No	Absence of respiratory tract disease	11 days	
A25	Not stated	Not stated	19	Not stated	Not stated	19	0.0	Plasma glucose	Yes, data not given	None usable	Three weeks after parturition	Assumes that half of the 38 randomised animals received homeopathy or placebo. 'Main outcome' decided on coin toss
A27	94	31	125	94	31	125	0.0	Parturition	No	Parturition	Not stated	Sperm was treated

CI Confidence interval, CMT California mastitis test, h Homeopathy group(s), n Number, p Placebo group(s), sd Standard deviation

TABLE 3: Risk-of-bias judgements made in the 18 placebo-controlled RCTs

Trial	I. Sequence generation	II. Allocation concealment	IIIA. Blinding: personnel	IIIB. Blinding: outcome assessors	IV. Complete outcome data	V. Outcome reporting	VI. Free of other bias (excl. funding)	Number of domains for which Cochrane criteria fulfilled			Risk of bias (excluding assessment of vested interest)	Trial with reliable evidence
								Y	U	N		
Individualised homeopathy/treatment												
A01	Y	Y	Y	Y	Y	Y	Y	7	0	0	Low	Yes
A02	Y	U	N	N	Y	Y	U	3	2	2	High	No
Non-individualised homeopathy/treatment												
A05	U	U	Y	Y	U	N	N	2	3	2	High	No
A09	U	U	Y	Y	Y	Y	N	4	2	1	High	No
A04	Y	Y	Y	Y	Y	Y	U	6	1	0	Unclear	Yes
A11	N	N	Y	Y	Y	Y	N	4	0	3	High	No
A06	N	N	Y	U	N	Y	U	2	2	3	High	No
A28	U	U	N	U	U	Y	U	1	5	1	High	No
A03	U	U	U	U	N	N	N	0	4	3	High	No
A08	Y	U	Y	Y	U	Y	Y	5	2	0	Unclear	No
A10	U	N	U	U	Y	Y	Y	3	3	1	High	No
A07	Y	U	Y	Y	U	Y	Y	5	2	0	Unclear	No
Non-individualised homeopathy/prophylaxis												
A23	N	N	Y	Y	Y	Y	Y	5	0	2	High	No
A24	Y	U	Y	Y	Y	Y	Y	6	1	0	Unclear	Yes
A26	U	U	Y	Y	U	Y	Y	4	3	0	Unclear	No
A22	Y	U	N	N	U	Y	N	2	2	3	High	No
A25	U	U	N	U	U	Y	U	1	5	1	High	No
A27	U	U	Y	Y	Y	Y	Y	5	2	0	Unclear	No

Criteria fulfilled for domains Y Yes, U Unclear, N No

of bias; six trials had uncertain risk of bias; and the remaining 11 trials were judged to be at high risk of bias, some of them failing the assessment criteria in more than one domain.

Of the seven trials not deemed to be at high risk of bias, four of them failed to meet the criteria for reliable evidence. These were Holmes and others (2005), Hielm-Björkman and others (2009), Guajardo-Bernal and others (1996) and Soto and others (2010). One of the three remaining (reliable) trials had potential vested interest due to funding source (Cracknell and Mills 2008) and so was not reflected in the primary conclusions.

Considering the assessments overall, high risk of bias was evident across all domains (Table 3). Domains IIIA (personnel blinding) and domain VI (other biases, which most frequently were connected with extreme data imbalances) were at high risk of bias particularly frequently. For randomisation (domain I), only seven of the 18 trials had low risk of bias. A problem that was frequently encountered was the lack of detail or clarity provided in the original papers; allocation concealment (domain II) was associated with the greatest rate of uncertainty in assessment.

Trials at low/uncertain risk of bias

The summary statistics for each of the seven RCTs that were assessed to be at low/uncertain risk of bias are presented in Table 4. The direction of effect was towards homeopathy in each of the six trials from which data could be extracted. The seventh trial in this category (Holmes and others 2005) contained logarithmic data. Due to the diversity of medical conditions, species and types of homeopathic intervention displayed in these six trials, and the fact that analysis was limited to data from trials at low/unclear risk of bias, it was not considered appropriate to carry out meta-analysis on disease-specific treatment or prophylaxis.

Trials designated as having reliable evidence and being free of vested interest

Only two trials were considered to have reliable evidence and contributed to the primary conclusions (that is, low/uncertain risk of bias overall, with low risk of bias for each of Cochrane domains I, IIIA, IIIB and IV, and also without overt vested interest due to funding source); these were Hektoen and others (2004) and Camerlink and others (2010). An additional facet of study design should be noted in each case: the Hektoen RCT was a semi-crossover trial, whose data were extracted for the precrossover timepoint; and the Camerlink RCT involved treating sows but evaluating piglets.

These two trials analysed different medical conditions, species and categories of intervention, and so a meta-analysis was not appropriate.

As displayed in Table 4, the Hektoen trial (A01) showed a non-significant treatment effect in cattle with mastitis (SMD −0.31, 95 per cent CI −0.97 to 0.34, P=0.35), while the Camerlink trial (A24) showed a statistically significant effect in the prophylaxis of diarrhoea in piglets (OR 3.89, 95 per cent CI 1.19 to 12.68, P=0.02).

Trials at high risk of bias

The 11 trials that were judged to be at high risk of bias are presented in Table 5. The direction of effect was towards homeopathy in five trials (three statistically significantly, though highly variable and imprecise in the magnitude of effect size) and towards placebo in four (none statistically significantly). Data were not extractable from the remaining two trials.

Discussion

Although six trials with extractable data were judged to be at low/unclear risk of bias, their diverse characteristics prevented the

TABLE 4: Trials at low or unclear risk of bias

Trial	Condition	Species	Outcome measure	Data extracted		Summary effect measure	Effect size (95 per cent CI)	Direction of effect	P value
				Homeopathy	Placebo				
Individualised homeopathy/treatment									
A01	**Mastitis**	**Cattle**	**Acute mastitis score**	**Mean, 12.2, sd 4.72, n=21**	**Mean 13.7, sd 4.60, n=16**	**SMD**	**-0.31 (-0.97, 0.34)**	**Homeopathy**	**0.35**
Non-individualised homeopathy/treatment									
A04	***Fear of firework noises***	***Dogs***	***Improved (that is reduced) fear response***	***25 of 34***	***26 of 38***	***OR***	***1.28 (0.46, 3.57)***	***Homeopathy***	***0.63***
A08	Mastitis	Cattle	None usable	X	X	X	X	X	X
A07	*Osteoarthritis*	*Dogs*	*Improved mobility index*	*10 of 14*	*4 of 15*	*OR*	*6.88 (1.35, 35.06)*	*Homeopathy*	*0.02*
Non-individualised homeopathy/prophylaxis									
A24	**Diarrhoea**	**Pigs**	**Absence of diarrhoea per litter**	**17 of 24**	**10 of 26**	**OR**	**3.89 (1.19, 12.68)**	**Homeopathy**	**0.02**
A26	Growth rate	Pigs	Piglets' final body weight	Mean 9.4, sd 2.66, n=39	Mean, 8.2, sd 2.66, n=40	SMD	0.45 (0.00, 0.89)	Homeopathy	0.05
A27	Reproductive performance	Pigs	Parturition	69 of 94	22 of 31	OR	1.13 (0.46, 2.78)	Homeopathy	0.79

CI Confidence interval, OR Odds ratio, sd Standard deviation, SMD Standardised mean difference
Bold text indicates trials deemed reliable; Italic text indicates trials with a potential risk of bias due to funding source (see also Table 1)

application of meta-analytical methods to examine disease-specific effects. Each of these six trials had a direction of treatment effect towards homeopathy, three of them significantly ($P \leq 0.05$). However, such 'vote counting' masks a lack of robustness in the data, the small sample size per trial contributing to a wide confidence interval with lower limit approaching null effect. A meta-analysis of all six trials together (irrespective of species, medical condition, outcome measure or type of homeopathic intervention), following the combined analytical approach reported by Linde and others (1997) and Shang and others (2005), was outside the scope of the current review. Sensitivity analyses on relevant groups of trials, reflecting the full range of risk of bias across all 18 RCTs, is the subject of a separate paper (Mathie and Clausen, in press).

Only two trials did not have high risk of bias and contained reliable evidence that was free from vested interest; the disparate nature of these trials again prevented meta-analysis. It is the evidence separately from those two trials, therefore, that forms the basis of the primary conclusions of this review: Hektoen and others (2004) (individualised treatment using unspecified homeopathic potencies of acute bovine mastitis); and Camerlink and others (2010) (prophylaxis of porcine

TABLE 5: Trials at high risk of bias

Trial	Condition	Species	Outcome measure	Data extracted		Summary effect measure	Effect size (95 per cent CI)	Direction of effect	P value
				Homeopathy	Placebo				
Individualised homeopathy/treatment									
A02	Mastitis	Cattle	Totally cured quarters	8 of 58	4 of 43	OR	1.56 (0.44, 5.56)	Homeopathy	0.49
Non-individualised homeopathy/treatment									
A05	*Diarrhoea*	*Cattle*	*Duration of diarrhoea (days)*	*Mean 3.1, sd 1.72, n=24*	*Mean 2.9, sd 1.72, n=20*	*SMD*	*0.11 (-0.48, 0.71)*	*Placebo*	*0.71*
A09			*Animals with 'pasty' stools*	*5 of 6*	*8 of 9*	*OR*	*0.63 (0.03, 12.41)*	*Placebo*	*0.76*
A11	*Induction of farrowing*	*Pigs*	*Presence of uterine contraction*	*14 of 18*	*0 of 23*	*OR*	*151.4 (7.58, 3024)*	Homeopathy	*0.001*
A06	Infertility	Cattle	Gestating cows	49 of 58	47 of 56	OR	1.04 (0.38, 2.85)	Homeopathy	0.94
A28			*Held to first service*	*20 of 50*	*11 of 26*	*OR*	*0.91 (0.35, 2.38)*	*Placebo*	*0.85*
A03	*Mastitis*	*Cattle*	*None usable*	*X*	*X*	*X*	*X*	*X*	*X*
A10			Unaffected quarters	34 of 51	15 of 52	OR	4.93 (2.14, 11.38)	Homeopathy	0.0002
Non-individualised homeopathy/prophylaxis									
A23	*Endometritis*	*Cattle*	*Absence of endometritis*	*231 of 417*	*126 of 200*	*OR*	*0.73 (0.52, 1.03)*	*Placebo*	*0.07*
A22	*Infectious diseases (respiratory)*	*Pigs*	*Absence of respiratory tract disease*	*436 of 480*	*411/480*	*OR*	*1.66 (1.11, 2.49)*	Homeopathy	*0.01*
A25	Metabolic disturbance postpartum	Goats	None usable	X	X	X	X	X	X

CI Confidence interval, OR Odds ratio, sd Standard deviation, SMD Standardised mean difference. Italic text indicates trials with a potential risk of bias due to funding source (see also Table 1)

diarrhoea with an ultra-dilution of the homeopathic preparation Coli).

Camerlink reported a large, though imprecise, effect size that was statistically significant, in favour of homeopathy; the smaller effect size reported by Hektoen was not statistically significant. The idiosyncrasies of study design in these two trials (indirect treatment of piglets via the sow; semi-crossover RCT) should also be noted. From the only two trials that inform the primary conclusions, therefore, there is modest evidence that homeopathic Coli has a prophylactic effect on porcine diarrhoea and that individualised homeopathy is not more beneficial than placebo in the treatment of bovine mastitis. It is not possible to generalise from these two divergent findings to other medical targets of veterinary homeopathic treatment or prophylaxis, for which there is no reliable (or any) research evidence.

The authors are confident that the risk-of-bias assessment approach was fair and rigorous, always erring on the side of stringency. Indeed, the definition of an RCT with reliable evidence closely approximates that used by Shang and others (2005) to designate a trial of 'higher methodological quality'; moreover, source of research funding (vested interest) was also taken into account as a matter of key importance in these assessments. Given that the 18 eligible trials were published in peer-reviewed journals – arguably therefore representing the 'best' of such RCT research in veterinary homeopathy – the inability of our findings to yield broader-based conclusions may disappoint homeopathy's advocates and critics alike. Neither gloom nor glee is indicated here for either side of the polarised argument: matters will be settled only in the event of more and much better-quality research. Similar cautionary notes about the limited quality and clarity of the available evidence in homeopathy were applied in a recent Cochrane review – involving one of the current authors – of homeopathic Oscillococcinum for influenza in humans (Mathie and others 2012a).

Shortcomings of the papers included in this review were concerned particularly with randomisation, allocation concealment, blinding and source of funding. Such failings were undoubtedly contributory to the extraordinarily variable results provided by the 11 trials that were assessed to be at high risk of bias. A further problem was the unclear original reporting of the key data, particularly for standard deviation of a continuous measure: in such cases, the use of recognised Cochrane methods to calculate or estimate the sd enabled the otherwise unusable findings of some trials to be included in the data presentation (see Tables 2, 4 and 5). Deficiencies in RCTs of conventional veterinary medicine are also well recognised, including the potential relationship between funding source and positive outcome reporting (Wareham and others 2013).

The use of a single, hierarchy-based, outcome measure per trial harmonises with the method adopted in major systematic reviews of homeopathy RCTs in humans (Linde and others 1997, Shang and others 2005), as well as in the authors' own study protocol for meta-analysis of RCTs in human homeopathy (Mathie and others 2013) and in quality assessment of RCTs in conventional medicine (Hartling and others 2009). Some commentators have previously expressed concern that trials in homeopathy often use irrelevant or subjective outcomes (Merrell and Shalts 2002). None of the main outcome measures used in this analysis can be regarded as clinically irrelevant: only two (fear response to fireworks [Cracknell and Mills 2008] and 'pasty' stools [Kayne and Rafferty 1994]) can be regarded as subjective. Outcome measures that can be regarded as surrogate only featured in trials whose data proved to be not extractable for analysis (Andersson and others 1997, Holmes and others 2005, Danieli and others 2009). It was noteworthy that 16 of the 18 RCTs assessed here did not designate a 'main' or 'primary' outcome measure and this concern corresponded with the absence of a prospective power calculation to determine the appropriate sample size of trials.

The deficient nature of the current RCT literature in veterinary homeopathy indicates a clear need for further primary research investigation, whether in the context of individualised or non-individualised veterinary prescribing. New research of this nature can be informed by research-targeted observational studies on the outcomes of homeopathic treatment in cats, dogs and horses (Mathie and others 2010a, b). Naturally, such RCTs should be independently funded and strive for reliable evidence, and they should also optimise the model validity of the homeopathic intervention as state-of-the-art (Mathie and others 2012c). An updated search of peer-reviewed RCTs published since an original literature analysis in 2011 revealed only one new placebo-controlled trial (Notz and Hässig 2013). While this means that this systematic review is barely compromised by the absence of up-to-date findings, it also illustrates the near-static nature of this field of research. The authors are currently progressing a separate systematic review of veterinary RCTs in which the control group was a comparator other than placebo.

Although few in number (as well as deficient in quality), the preponderance of homeopathy RCTs in livestock might reflect the needs of the organic farming community, especially in the European Union (IMPRO 2012). The very small number of homeopathy RCTs in companion animals might reflect the difficulty of recruiting sufficient numbers of subjects for individualised treatment or prophylaxis, which necessitates long consultation times with each animal and its owner. The dearth of RCTs in individualised homeopathy per se is consistent with this conjecture.

Conclusions

From 18 RCTs in total, low or unclear risk of bias was ascribed to seven diverse trials, two of which were judged to contain reliable evidence and were free of vested interest due to funding source. Mixed findings in these two trials preclude generalisable conclusions about efficacy of a particular homeopathic medicine or the impact of individualised homeopathic intervention in any given medical condition in animals. There is an obvious need for new and higher quality research.

Acknowledgements

The authors would like to thank Elizabeth Baitson (British Homeopathic Association) for statistical support and Daniela Hacke (Karl und Veronica Carstens-Stiftung) for library assistance.

Conflict of interest statement

As a research physiologist (RTM) and a biologist (JC), each of us is employed by a homeopathy charity to clarify and extend an evidence base in homeopathy. We have applied the normal high standards of scientific method in the conduct of the work and of complete and transparent reporting in the write-up of the paper.

References

ALBRECHT, H. & SCHÜTTE, A. (1999) Homeopathy versus antibiotics in metaphylaxis of infectious diseases: a clinical study in pig fattening and its significance to consumers. *Alternative Therapies in Health and Medicine* **5**, 64-68

ANDERSSON, R., MORCILLO, L. L. & SOMMER, H. (1997) Untersuchungen über den Einsatz von homöopathischen Arzneimitteln bei der Behandlung und Prophylaxe subklinischer Mastitiden von Milchkühen [Treatment and prophylaxis of subclinical mastitis with homeopathic drugs]. *Tierärztliche Umschau* **52**, 407-412

ARLT, S., PADBERG, W., DRILLICH, M. & HEUWIESER, W. (2009) Efficacy of homeopathic remedies as prophylaxis of bovine endometritis. *Journal of Dairy Science* **92**, 4945-4953

BAKER, S., BOOTH, C., TAYLOR, N., GOUGH, A. & KERR, M. (2005) Homeopathic veterinary medicine. *Veterinary Record* **157**, 390-391

BELL, I. R. & SCHWARTZ, G. E. (2013) Adaptive network nanomedicine: an integrated model for homeopathic medicine. *Frontiers in Bioscience* **S5**, 685-708

CAMERLINK, I., ELLINGER, L., BAKKER, E. J. & LANTINGA, E. A. (2010) Homeopathy as replacement to antibiotics in the case of *Escherichia coli* diarrhoea in neonatal piglets. *Homeopathy* **99**, 57-62

CRACKNELL, N. R. & MILLS, D. S. (2008) A double-blind placebo-controlled study into the efficacy of a homeopathic remedy for fear of firework noises in the dog (*Canis familiaris*). *Veterinary Journal* **177**, 80-88

DANIELI, P. P., LACETERA, N., BERNABUCCI, U. & RONCHI, B. (2009) Conventional and homeopathic treatments in late pregnant goats: effects on metabolic status and immune response. *Italian Journal of Animal Science* **8**, 613-615

DEEKS, J. J., HIGGINS, J. P. T. & ALTMAN, D. G. (2011) Analysing data and undertaking meta-analyses. In Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0. Eds J. P. T. Higgins, S. Green. The Cochrane Collaboration

DE VERDIER, K., ÖHAGEN, P. & ALENIUS, S. (2003) No effect of a homeopathic preparation on neonatal calf diarrhoea in a randomised double-blind, placebo-controlled clinical trial. *Acta Veterinaria Scandinavica* **44**, 97-101

FIDELAK, C. H., KLOCKE, P. & HEUWIESER, W. (2007) Homöopathische Prophylaxe in der Bestandsbetreuung von Milchkühen. Teil 1 – Fruchtbarkeit [Homeopathic prophylaxis in dairy cows on an organic farm. Part 1 – fertility]. *Deutsche Tierärztliche Wochenschrift* **114**, 268-274

GUAJARDO-BERNAL, G., SEARCY-BERNAL, R. & SOTO-AVILA, J. (1996) Growth-promoting effect of Sulphur 201c in pigs. *British Homeopathic Journal* **85**, 15-16

HARTLING, L., OSPINA, M., LIANG, Y., DRYDEN, D. M., HOOTON, N., SEIDA, J. K. & KLASSEN, T. P. (2009) Risk of bias versus quality assessment of randomised

controlled trials: cross sectional study. *BMJ* **339**, b4012
HEKTOEN, L. (2005) Homeopathic veterinary medicine. *Veterinary Record* **157**, 391-392
HEKTOEN, L., LARSEN, S., ØDEGAARD, S. A. & LØKEN, T. (2004) Comparison of homeopathy, placebo and antibiotic treatment of clinical mastitis in dairy cows – methodological issues and results from a randomized-clinical trial. *Journal of veterinary medicine. A, Physiology, pathology, clinical medicine* **51**, 439-446
HIELM-BJÖRKMAN, A., TULAMO, R. M., SALONEN, H. & RAEKALLIO, M. (2009) Evaluating complementary therapies for canine osteoarthritis – Part II: a homeopathic combination preparation (Zeel). *Evidence-based Complementary and Alternative Medicine* **6**, 465-471
HIGGINS, J. P. T. & ALTMAN, D. G. (2011) Assessing risk of bias in included studies. Cochrane Handbook for Systematic Reviews of Interventions. In Version 5. 1. 0. Eds J. P. T. Higgins, S. Green. The Cochrane Collaboration
HIGGINS, J. P. T. & DEEKS, J. J. (2011) Selecting studies and collecting data. Cochrane Handbook for Systematic Reviews of Interventions. In Version 5.1.0. Eds J. P. T. Higgins, S. Green. The Cochrane Collaboration
HIGGINS, J. P. T., DEEKS, J. J. & ALTMAN, D. G. (2011) Special topics in statistics. In Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0. Eds J. P. T. Higgins, S. Green. The Cochrane Collaboration
HILL, P. B., HOARE, J., LAU-GILLARD, P., RYBNICEK, J. & MATHIE, R. T. (2009) Pilot study of the effect of individualised homeopathy on the pruritus associated with atopic dermatitis in dogs. *Veterinary Record* **164**, 364-370
HOLMES, M. A., COCKCROFT, P. D., BOOTH, C. E. & HEATH, M. F. (2005) Controlled clinical trial of the effect of a homoeopathic nosode on the somatic cell counts in the milk of clinically normal dairy cows. *Veterinary Record* **156**, 565-567
IMPRO (2012) Impact matrix analysis and cost-benefit calculations to improve management practices regarding health status in organic dairy farming: manageability of alternative treatments. www.impro-dairy.eu/index.php/fr/2012-10-04-16-42-51/workpackages/9-nicht-kategorisiert/80-wp4-manageability-of-alternative-treatments. Accessed April 19, 2013
KAYNE, S. & RAFFERTY, A. (1994) The use of Arsenicum album 30c to complement conventional treatment of neonatal diarrhoea ('scours') in calves. *British Homeopathic Journal* **83**, 202-204
LINDE, K., CLAUSIUS, N., RAMIREZ, G., MELCHART, D., EITEL, F., HEDGES, L. V. & JONAS, W. B. (1997) Are the clinical effects of homoeopathy placebo effects? A meta-analysis of placebo-controlled trials. *Lancet* **350**, 834-843
MATHIE, R. T., BAITSON, E. S., HANSEN, L., ELLIOTT, M. F. & HOARE, J. (2010a) Homeopathic prescribing for chronic conditions in feline and canine veterinary practice. *Homeopathy* **99**, 243-248
MATHIE, R. T., BAITSON, E. S., HANSEN, L., ELLIOTT, M. F. & HOARE, J. (2010b) Homeopathic prescribing for chronic conditions in equine veterinary practice in the UK. *Veterinary Record* **166**, 234-238
MATHIE, R. T. & CLAUSEN, J. (in press) Veterinary homeopathy: meta-analysis of randomised placebo-controlled trials. *Homeopathy*, accepted for publication.
MATHIE, R. T., FRYE, J. & FISHER, P. (2012a) Homeopathic Oscillococcinum® for preventing and treating influenza and influenza-like illness. *Cochrane Database of Systematic Reviews* **12**, CD001957
MATHIE, R. T., HACKE, D. & CLAUSEN, J. (2012b) Randomised controlled trials of veterinary homeopathy: characterising the peer-reviewed research literature for systematic review. *Homeopathy* **101**, 196-203
MATHIE, R. T., LEGG, L. A., CLAUSEN, J., DAVIDSON, J. R. T., LLOYD, S. M. & FORD, I. (2013) Systematic review and meta-analysis of randomised, placebo-controlled, trials of individualised homeopathic treatment: study protocol. www.britishhomeopathic.org/export/sites/bha_site/research/Study_protocol_for_systematic_review.pdf. Accessed April 19, 2013
MATHIE, R. T., RONIGER, H., VAN WASSENHOVEN, M., FRYE, J., JACOBS, J., OBERBAUM, M., BORDET, M. F. & OTHERS (2012c) Method for appraising model validity of randomised controlled trials of homeopathic treatment: multi-rater concordance study. *BMC Medical Research Methodology* **12**, 49
MERRELL, W. C. & SHALTS, E. (2002) Homeopathy. *Medical Clinics of North America* **86**, 47-62
MOHER, D., LIBERATI, A., TETZLAFF, J., ALTMAN, D. G. & THE PRISMA GROUP (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. *Annals of Internal Medicine* **151**, 1-7
NOTZ, C. & HÄSSIG, M. (2013) Zur Wirksamkeit einer homöopathischen Mastitisprophylaxe zum Trockenstellen und Abkalben beim Rind [Efficiency of a homeopathic prophylaxis in bovine mastitis during dry-off and parturition]. *Schweizer Archiv für Tierheilkunde* **155**, 405-409
OVERALL, K. L. & DUNHAM, A. E. (2009) Homeopathy and the curse of the scientific method. *Veterinary Journal* **180**, 141-148
RUTTEN, L., MATHIE, R. T., FISHER, P., GOOSSENS, M. & VAN WASSENHOVEN, M. (2013) Plausibility and evidence: the case of homeopathy. *Medicine, Health Care, and Philosophy* **16**, 525-532
SCHÜNEMANN, H. J., OXMAN, A. D., VIST, G. E., HIGGINS, J. P. T., DEEKS, J. J., GLASZIOU, P. & GUYATT, G. H. (2011) Interpreting results and drawing conclusions. In Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0. Eds J. P. T. Higgins, S. Green. The Cochrane Collaboration
SEARCY, R., REYES, O. & GUAJARDO, G. (1995) Control of subclinical bovine mastitis. Utilization of a homoeopathic combination. *British Homeopathic Journal* **84**, 67-70
SHANG, A., HUWILER-MUNTENER, K., NARTEY, L., JUNTHERAPIESI, P., DORIG, S., STERNE, J. A., PEWSNER, D. & EGGER, M. (2005) Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. *Lancet* **366**, 726-732
SOTO, F. R. M., VUADEN, E. R., PAULO COELHO, C., BONAMIN, L. V., AZEVEDO, S. S., BENITES, N. R., VISINTIN, J. A. & OTHERS (2010) Reproductive performance of sows inseminated with diluted semen treated with homeopathic medicine. *International Journal of High Dilution Research* **9**, 51-57
SWAYNE, J. (2000) International Dictionary of Homeopathy. Churchill Livingstone
WAREHAM, K., DEAN, R., GRINDLAY, D., BRENNAN, M. & HYDE, B. (2013) Bias in veterinary clinical trials. www.nottingham.ac.uk/cevm/evidence-synthesis/assessing-quality/bias-in-veterinary-clinical-trials.aspx. Accessed September 24, 2013
WERNER, C., SOBIRAJ, A. & SUNDRUM, A. (2010) Efficacy of homeopathic and antibiotic treatment strategies in cases of mild and moderate bovine clinical mastitis. *Journal of Dairy Research* **77**, 460-467
WORLD HEALTH ORGANIZATION (2002) Towards a Common Language for Functioning, Disability and Health: ICF – The International Classification of Functioning, Disability and Health. www.who.int/classifications/icf/training/icfbeginnersguide.pdf. Accessed April 19, 2013.
WILLIAMSON, A. V., MACKIE, W. L., CRAWFORD, W. J. & RENNIE, B. (1995) A trial of Sepia 200c. Prevention of anoestrus problems in dairy cows. *British Homeopathic Journal* **84**, 14-20
WOLTER, H. (1966) Arzneiwirkungsprüfung an Caulophyllum D 30: ein doppelter Blindversuch [Drug efficacy testing of Caulophyllum D 30. A double-blind trial]. *Der Praktische Tierarzt* **47**, 431-432, 496-501

Veterinary Record

Veterinary homeopathy: systematic review of medical conditions studied by randomised placebo-controlled trials

Robert T. Mathie and Jürgen Clausen

Veterinary Record 2014 175: 373-381
doi: 10.1136/vr.101767