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### ORIGINAL PAPER

# Homeopathic prescribing for chronic conditions in feline and canine veterinary practice

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Introduction: The peer-review literature contains no controlled clinical research of homeopathy in cats and very little in dogs.

Main objective: To collect clinical outcomes data systematically from individualised homeopathic treatment of cats and dogs that would help to inform controlled research in feline and canine homeopathy.

Methods: Twenty-one homeopathic veterinary surgeons recorded data systematically from consecutive feline and canine patients over a 12-month period. Records included: date; patient and owner identity (anonymised); medical problem treated; whether new or follow-up (FU) appointment; chronic or acute condition; owner-assessed clinical outcome (7-point scale, range -3 to +3) compared with first appointment.

Results: Data from 400 cats comprised a total of 372 individual chronic problems, of which 270 had FU assessment. Data from 1504 dogs comprised a total of 1408 individual chronic problems, of which 1070 had FU assessment. In both species, 22% of FUs in chronic cases received conventional medicines concurrently. In cats, 117 different chronic medical conditions in total were treated with homeopathy. Five of those conditions included ≥20 cases, in which owner-reported outcomes (in decreasing rank order of frequency) were: dermatitis (69.6% patients with +2 or +3 outcome, 0% patients with -2 or -3 outcome); renal failure (57.1%, 14.3%); overgrooming (57.1%, 7.2%); arthritis (80.0%, 0%); hyperthyroidism (66.7%, 0%). In dogs, of 301 different chronic medical conditions treated in total, those most commonly recorded (≥20 cases) were: dermatitis (66.2% with +2 or +3 outcome, 5.4% with -2 or -3 outcome); arthritis (80.2%, 0.8%); pyoderma (75.8%, 0%); colitis (85.2%, 0%); fear (31.6%, 0%); epilepsy (63.6%, 4.5%); otitis externa (72.7%, 0%); diarrhoea (68.2%, 0%); urinary incontinence (73.7%, 0%); aggression (57.1%, 0%); spondylosis (81.0%, 0%); lymphoma (40.0%, 6.7%). Conclusions: A programme of controlled research in veterinary homeopathy for these feline and canine conditions is clearly indicated. Homeopathy (2010) 99, 243-248.

Keywords: Homeopathy; Clinical outcomes; Arthritis; Dermatitis; Cats; Dogs

### Introduction

There are currently 80–100 veterinary surgeons in the United Kingdom who prescribe homeopathic medicines

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in first-opinion or referral practice. Key facts about homeopathy and its research evidence base are summarised elsewhere. Positive research findings in veterinary homeopathy have been reported in the peer-review literature, but these are currently limited to non-controlled studies and to randomised controlled trials (RCTs) focused mainly on farm livestock.

In the peer-reviewed literature to date there have been, to our knowledge, no reports of RCTs of homeopathy in cats, and only three in dogs. 8-10 The purpose of the present study was to collect systematic clinical outcomes data

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from individualised homeopathic treatment of cats and dogs, across a wide spectrum of clinical diagnoses, that would be capable of informing new and relevant RCTs of homeopathy in these species. The study arose directly from a pilot project in which 8 vets collected appointments data over a 6-month period. The present study included 21 practitioners in a 12-month period of data collection, in which particular focus was on chronic medical problems, while also accounting for concurrent use of both conventional and other complementary medicine.

The specific aims of the study were:

- 1. To gain insight into the chronic feline and canine problems that vets in the UK treat using homeopathy.
- In follow-up (FU) appointments, to determine ownerassessed change in severity of the chronic medical problems treated.
- 3. Thus to identify any promising patterns of chronic disease and clinical responses that would help to target future controlled research in feline and canine homeopathy.

### **Methods**

Twenty-one vets contributed to the study (19 in England, 2 in Scotland): 6 first-opinion practices, 10 referral practices, 5 first-opinion/referral practices. Each vet also had the homeopathic qualification Veterinary Member of the Faculty of Homeopathy (VetMFHom) or Veterinary Fellow of the Faculty of Homeopathy (VetFFHom) or Certificate of the International Association for Veterinary Homeopathy (Cert IAVH). The 21 vets collected data from consecutive homeopathy appointments in cats and dogs during the period 1 May 2007 to 30 April 2008. The study ran simultaneously with equivalent data collection in horses. <sup>12</sup>

A spreadsheet, based on the pilot study, 11 enabled recording of all consecutive homeopathy appointments under the following column headings (cases of homeopathic prophylaxis or 'immunisation' were not recorded): (1) appointment date (day, month); (2) unique patient identity number; (3) patient's name and owner's surname initial; (4) sex of patient; (5) the main problem being treated (non-listed diagnoses or descriptions could be inserted by vets as required); (6) whether problem is 'chronic' or 'acute'; (7) whether case referred, at some stage, to a specialist recognised by the Royal College of Veterinary Surgeons (RCVS); (8) whether, in relation to the previous 12 months, this is a new or a FU appointment for the same problem; (9) owner-assessed change in the treated problem at FU compared with the *first* homeopathic consultation, using 7-point outcome scale (see below); (10) homeopathic medicine/s prescribed at this consultation; (11) whether any conventional treatment (prescription drugs, dietary advice, etc.) for this condition; (12) whether other complementary/alternative medicine (CAM) treatment currently for this condition (acupuncture, etc.). A medical problem was classified as chronic if it had been apparent for at least three months. An acute flare-up of a chronic condition was labelled 'chronic'.

Owner-assessed clinical outcomes were ascertained and recorded as previously described.  $^{11,12}$  Owners' responses were transcribed by the vet as follows: major deterioration = -3; moderate deterioration = -2; mild deterioration = -1; no change or unsure = 0; mild improvement = +1; moderate improvement = +2; major improvement = +3.

The Chair of the South Bedfordshire Research Ethics Committee (REC) advised that a study of this type did not require REC approval.

### Methods of spreadsheet analysis

Upon receipt of final spreadsheets at the end of the project, the original data were filtered for missing or erroneous data and rectified where possible in consultation with the vet concerned. Terminology for non-listed medical conditions was reconciled to eliminate duplications or ambiguity. For cats, the terms 'atopic dermatitis' (n = 17)cases), 'allergic dermatitis' (n = 8), 'miliary dermatitis' (n = 5), 'dermatitis' (n = 3), and 'eczema' (n = 1) were all analysed together under the single heading 'dermatitis'. For dogs, the terms 'allergic dermatitis' (n = 54), 'atopic dermatitis' (n = 135) and 'dermatitis' (n = 2) were all analysed together under the single heading 'dermatitis'; pyoderma (n = 42) remained a separately analysed entry. In cases where more than a single medical problem was listed together at a given appointment, the first-named was the single term used for data analysis.

Appointments data from all 21 vets were consolidated, per species, into a master spreadsheet. 12 Analysis of outcomes focused on 'last' appointments (and for chronic cases) only - i.e. on the number of individual feline or canine conditions treated, irrespective of whether they were previously treated by the vet once, twice or more often. The outcome score recorded at this last FU appointment per case recorded during the 12 months was thus the single value analysed and presented for that animal within the descriptive statistics below. Likewise, the homeopathic medicine used at this last recorded appointment was the single one used per case in the analysis. Statistical comparison of proportions was carried out by Chi-square test (Microsoft Excel);  $P \le 0.05$  was regarded as statistically significant. Correlation analysis was carried out (Excel) using Spearman's rank difference correlation statistic, ρ.

## **Results**

### Cats

Demographic data: A total of 903 homeopathic appointments were recorded for feline patients over the 12-month period. These appointments represented a total of 445 individual feline conditions, 45 of which applied to cats that were also presented for treatment on a separate visit for a different medical condition; 400 individual animals were therefore examined in total. The male:female ratio was 48%:52%. A total of 73 of the 445 individual feline problems were acute in nature, the most frequently

Table 1 Summary of outcomes at last recorded FU appointment in most frequently treated (n ≥ 20) chronic conditions in cats

Chronic condition	No. of cases	No. of last FUs	−2 or −3 score, %	−1 or 0 or +1 score, %	+2 or +3 score, %	Specialist referral, %	Conv. treatment, %	Other CAM treatment, %
Dermatitis (12 vets)*	34	23	0.0	30.4	69.6	13.0	13.0	0.0
Renal failure (11)	27	21	14.3	28.6	57.1	38.1	38.1	14.3
Overgrooming (12)	26	14	7.2	35.7	57.1	0.0	14.3	14.3
Arthritis (10)	21	15	0.0	20.0	80.0	40.0	26.7	40.0
Hyperthyroidism (8)	21	18	0.0	33.3	66.7	55.6	16.7	16.7
All Others (21)	243	179 <sup>†</sup>	5.0	31.3	62.0	18.4	22.3	10.6
Total	372	270	4.8	30.8	63.3	22.2	22.2	12.2

See text for description of outcome scoring system. Table includes percentages of cases where there had been referral to an RCVS-recognised specialist, or receiving conventional (conv.) or other CAM treatment concurrently.

recorded being abscess (n = 8) and conjunctivitis (n = 5). A total of 372 of the 445 problems were chronic in nature, and these are the feline cases that comprise the remainder of this paper. A total of 117 different individual chronic medical conditions were noted: the 5 most frequently seen (n  $\geq$  20 cases) are listed in Table 1. Each of another 112 chronic conditions was seen in fewer than 20 cases, of which the most frequently observed were diarrhoea (n = 14), rhinitis (n = 14) and colitis (n = 10).

The single homeopathic medicines most frequently used at the last recorded appointment per chronic case during the period of data collection were as follows: *Natrium muriaticum*, 21; *Arsenicum album*, 9: *Staphysagria*, 8. Another 76 different single medicine prescriptions were used overall, and any one of various different combinations of homeopathic medicines was recorded in 130 instances. There was little evidence of matching of a particular homeopathic medicine (or particular combination of medicines) with a specific medical condition. The limited evidence for such matching was 4/15 (26.6%) cases of arthritis treated with the combination *Rhus toxicodendron*, *Ruta graveolens* and *Arnica montana* (*RRA*), and 4/18 (22.2%) cases of hyperthyroidism treated with *Iodium*.

Clinical outcomes — chronic medical conditions: Of the 372 individual chronic cases, 102 were first appointments only and 270 had received at least one FU appointment. The last recorded FU appointment number for these 270 chronic cases varied between 2 and 10 (median, 2). The median number of last outcomes reported per month was 16, with a range of 12 (in May 2007, the first month of the study) to 41 (April 2008, the final month of the study). For the 270 last recorded FUs, a score of +2 or +3 (moderate or major improvement) was reported in 63.3%; a score of -2 or -3 (moderate or major deterioration) was recorded in 4.8%; little or no change (score of -1, 0 or +1) was noted in 30.8% (Table 1). There were missing outcomes at last appointment in 1.1% of cases.

High positive scores (+2 or +3) were achieved most notably (i.e. higher than the average, 63.3%, for all conditions) in arthritis, dermatitis and hyperthyroidism (Table 1). High positive scores were achieved less notably in overgrooming and renal failure, in which strongly negative scores (-2 or -3) were reported in a number of cases. For the 5 most frequently treated conditions, last outcomes

data per case were recorded at (median) appointment number 2 (for arthritis, hyperthyroidism, overgrooming, and renal failure) or appointment number 3 (for dermatitis). Overall, 16 of the 21 practitioners contributed outcomes data for the top five conditions (8–12 vets per specific condition; Table 1).

Of the 270 FU chronic cases overall, there were 60 (22.2%) that had been seen by an RCVS-recognised specialist, 60 (22.2%) that were receiving conventional medication (i.e. stated as 'less', 'same', 'more' or 'started'), and 33 (12.2%) where another complementary medical therapy was being provided concurrently with homeopathy (Table 1). Conventional medication was not used at all in 200 cases (74.1% of the total), and had been stopped by the last homeopathic appointment in 10 cases (3.7%). For the five most commonly treated chronic conditions, there was a high rate of specialist diagnosis in hyperthyroidism (55.6%) but none in overgrooming; in arthritis and renal failure there were high rates of conventional and complementary medical treatment (up to 40%), whereas in dermatitis the equivalent figures were considerably lower (up to 13%).

There was no significant difference between the rate of +2/+3 outcomes with and without the use of other CAM therapy (63.6% vs. 64.7%; P>0.05) or depending on whether or not there had been referral to an RCVS-recognised specialist (74.5% vs. 60.8%; P>0.05). Cats that received concurrent conventional treatment had a lower rate of +2/+3 scores than those that did not receive such treatment (52.5% vs. 68.1%; P<0.05). Use of conventional treatment correlated positively with a greater number of FU appointments ( $\rho$  = 0.90; mean 6% increase, per last appointment number, in the rate of use of conventional medicine).

### Dogs

Demographic data: A total of 3612 homeopathic appointments for canine patients were reported over the 12-month period. The 3612 appointments represented a total of 1740 canine conditions; 236 of those conditions applied to dogs that were also presented for treatment on a separate visit for a different medical condition, and so 1504 individual animals were examined in total.

<sup>\*</sup> Numeral in parentheses is number of practitioners reporting cases.

<sup>&</sup>lt;sup>†</sup> 3 Outcome scores missing.

The male:female ratio was 51%:49%. A total of 332 of the 1740 individual canine problems were acute in nature, the most frequently recorded being diarrhoea (n = 25), fear (n = 15) and false pregnancy (n = 13). A total of 1408 of the 1740 problems were chronic in nature, and these are the canine cases presented and discussed in the remainder of this report. A total of 301 different individual chronic medical conditions were noted: the 12 most frequently seen ( $n \ge 20$  cases) are listed in Table 2. Each of another 289 chronic conditions was seen in fewer than 20 cases; of those others the most frequently observed were renal failure (n = 18), hip dysplasia (n = 17), asthma/bronchitis (n = 16), chronic degenerative radiculomyelopathy (n = 16), Cushing's syndrome (n = 16), lameness (n = 15), mast cell tumour (n = 15), conjunctivitis (n = 14), anxiety (n = 12) and cruciate injury (n = 11).

The single homeopathic medicines most frequently used at the last appointment per chronic case during the period of data collection were as follows: *Pulsatilla*, 51; Sulphur, 31; Phosphorus, 28; Calc Flour, 23; Lycopodium, 22; Causticum, 21. Another 169 different single medicines were used in other cases, and any one of various different combinations of homeopathic medicines was recorded in 233 instances. Each combination preparation was a unique mix of 2-7 (median 2) different homeopathic medicines. As for cats, individualised homeopathic prescribing per dog was the norm. There was only limited evidence of matching of a particular homeopathic medicine (or combination of medicines) with a specific medical condition: within the top 12 most frequently followed-up chronic conditions, 4/19 (21.0%) cases of urinary incontinence were treated with Pulsatilla, 4/22 (18.8%) cases of diarrhoea with Lycopodium, 20/121 cases (16.5%) of arthritis with the combination medicine RRA, and 20/148 (13.5%) of cases of dermatitis with Pulsatilla.

Clinical outcomes — chronic medical conditions: Of the 1408 individual chronic canine cases, 335 were first appointments only and 1070 had received at least one FU appointment; 3 cases were not attributed by appointment type. The last recorded FU appointment number for these 1070 chronic cases varied between 2 and 13 (median, 2). The median number of last outcomes reported per month was 126, with a range of 70 (in May) to 256 (April). For the 1070 chronic follow-up cases, a score of +2 or +3 (moderate or major improvement) was recorded at last appointment in 68.9%; a score of -2 or -3 (moderate or major deterioration) was recorded in 2.6%; little or no change (score of -1, 0 or +1) was noted in 28.0% (Table 2); there were missing scores in 5 (0.5%) cases.

Outcome scores for each of the top twelve medical conditions are given in Table 2. High positive scores (+2 or +3) were achieved most notably (i.e. higher than the average, 68.9%, for all conditions) in arthritis, colitis, otitis externa, pyoderma, spondylosis and urinary incontinence. Within the twelve conditions, high positive scores were achieved much less notably in fear (31.6%) and lymphoma (40.0%). A small proportion of strongly negative scores (-2 or -3) was reported for each of dermatitis, epilepsy and lymphoma. For the top twelve conditions, last recorded outcomes data per case were reported at (median) appointment number 2 except for epilepsy and spondylosis which were recorded at (median) appointment number 3. Overall, all of the 21 practitioners contributed outcomes data for the top twelve conditions (6-19 vets per specific condition).

Of the 1070 FU chronic cases, there were 299 (27.9%) where there had been RCVS specialist referral, 236 (22.1%) who were receiving conventional medication at the last recorded appointment, and 277 (25.9%) in which another CAM treatment was being offered concurrently with homeopathy (Table 2). At the last recorded appointment, conventional medication was not being used in 814 cases (76.1%): it had never been used in 751 cases and

**Table 2** Summary of outcomes at last recorded FU appointment in most frequently treated ( $n \ge 20$ ) chronic conditions in dogs

Chronic condition	No. of cases	No. of last FUs	−2 or −3 score, %	-1 or 0 or +1 score, %	+2 or +3 score, %	Specialist referral, %	Conv. treatment, %	Other CAM treatment, %
Dermatitis (19 vets)*	191	148 <sup>†</sup>	5.4	27.7	66.2	29.1	19.6	10.8
Arthritis (16)	153	121 <sup>†</sup>	0.8	18.2	80.2	25.6	24.8	57.9
Pyoderma (12)	42	33	0.0	24.2	75.8	24.2	24.2	30.3
Colitis (13)	36	27	0.0	14.8	85.2	22.2	7.4	14.8
Fear (12)	34	19	0.0	68.4	31.6	0.0	10.5	15.8
Epilepsy (10)	30	22	4.5	31.8	63.6	27.3	31.8	22.7
Otitis externa (9)	29	22	0.0	27.3	72.7	27.3	9.1	22.7
Diarrhoea (9)	28	22	0.0	31.8	68.2	18.2	22.7	18.2
Urinary incontinence (14)	28	19	0.0	26.3	73.7	0.0	31.6	10.5
Aggression (9)	27	14	0.0	42.9	57.1	7.1	0.0	7.1
Spondylosis (6)	27	21	0.0	19.0	81.0	33.3	28.6	52.4
Lymphoma (10)	21	15	6.7	53.3	40.0	66.7	66.7	26.7
Áll Óthers (21)	762	<i>587</i> ‡	2.6	28.0	68.9	30.2	22.0	24.2
Total	1408	1070	2.6	28.0	68.9	27.9	<b>22.1</b> §	<b>25.9</b> <sup>  </sup>

See text for description of outcome scoring system. Table includes percentages of cases where there had been referral to an RCVS-recognised specialist, or receiving conventional (conv.) or other CAM treatment concurrently.

<sup>\*</sup> Numeral in parentheses is number of practitioners reporting cases.

<sup>1</sup> Outcome score missing.

<sup>&</sup>lt;sup>‡</sup> 3 Outcome scores missing.

<sup>§ 20 &#</sup>x27;Conv. treatment' entries missing in total, including 8 in top 12 conditions.

<sup>24 &#</sup>x27;Other CAM treatment' entries missing in total, including 11 in top 12 conditions.

had been stopped by the last homeopathic appointment in 63. The above overall percentages broadly typified the figures for any given chronic problem of the twelve most commonly treated (see Table 2). The main exceptions were: no specialist referral for fear or urinary incontinence; high rates of specialist referral and of conventional treatment in lymphoma; high rates of other CAM treatment in arthritis and spondylosis.

There was no difference between the rate of +2/+3 outcomes with and without the use of other CAM treatment (71.8% vs. 68.5%; P>0.05) and for the FU cases with and without specialist referral (73.2% vs. 67.2%; P>0.05). The rate of +2/+3 outcomes was significantly lower for the FU cases with concurrent conventional treatment than for those without (52.1% vs. 74.5%; P<0.001); dermatitis was the single condition mainly responsible for this overall finding (31.0% vs. 76.5%; P<0.001). Use of conventional treatment correlated positively with a greater number of FU appointments ( $\rho$  = 0.71; mean 2% increase, per last appointment number, in the rate of use of conventional medicine).

## **Discussion**

The outcomes reported here support and extend our pilot findings in regard to the medical problems treated and the outcomes associated with homeopathic treatment. In both cats and dogs, dermatitis was the condition most frequently treated with homeopathy. In cats, other commonly treated conditions were confirmed as renal failure and hyperthyroidism, while in dogs, arthritis, epilepsy and otitis externa were seen frequently once again. Newly prominent conditions were (in cats) arthritis and overgrooming and (in dogs) colitis, diarrhoea, fear, lymphoma, pyoderma, spondylosis, and urinary incontinence.

Owner-reported outcome scores of +2 or +3 were recorded overall in 63.3% of feline cases and in 68.9% of canine cases, similar to the 66.7% and 60.0% respectively in our earlier study. 11 In the present report, strongly positive outcomes in cats were again noted in hyperthyroidism and also in dermatitis and arthritis, though there was a high rate of conventional and/or complementary medical intervention concurrently in the latter condition. Lower rates of improvement were observed in renal failure and overgrooming, where there was also a notable incidence of strongly negative outcomes. In dogs, there was a higher improvement rate than previously in arthritis and otitis externa, 11 though concurrent other treatment was notable this time in both conditions. Owner-assessed responses to treatment for canine epilepsy were similar to those in the previous study. Low rates of improvement were noted in fear and lymphoma, with several poor outcomes also for the latter condition. These findings – the positive and the negative - now need to be confirmed or refuted by controlled research.

In comparison with our pilot study, the present data collection involved more practitioners and over a longer time period, with particular focus on chronic medical problems, and taking into account conventional prescriptions and use of complementary medicine. The project has thus identified more clearly a number of chronic medical problems of cats and dogs that are most frequently treated using homeopathy, as well as the changes reported by the owner in each case. Many of these medical problems can prove difficult to improve satisfactorily by conventional treatment; such conditions in human medicine have been termed 'effectiveness gaps'. 13 It is perhaps not surprising that the animals of both species who were receiving conventional treatment had lower rates of positive outcomes scores overall than those without such concomitant treatment: animals on conventional medication were likely to be cases that were especially difficult or intractable, and this supposition is supported in each species by the association found between a higher number of FU appointments per case and a greater usage of conventional medicine.

Positive bias in outcomes data is an inevitable consequence of study design that is neither controlled nor randomised, and our overall 63.3% (cats) and 68.9% (dogs) with +2/+3 outcomes require further comment. These findings are in line with the 50-68% recorded in equivalent observations in humans. 14-16 Nevertheless, we have no intention of overstating the conclusions from this type of study. Because of the deliberate absence of a control group, we are unable to take into account many possible confounding factors such as waxing and waning of symptoms over time or regression to the mean. In addition, about 25% of cases overall did not receive FU during the period of data collection; ownerassessed change in these animals is therefore unknown. Moreover, 'desire to please' is a normal facet of clinical information obtained directly from a client, and each owner will have differing views as to what constitutes moderate or major change in their pet's state of health. As in all our other systematic observational studies, including that in horses, <sup>12</sup> a causal relationship between homeopathy and clinical outcome is not an inference from this investigation.

Sceptics of homeopathy often argue that misdiagnosis can explain the apparent success of the therapy in diseases that are difficult to improve using conventional medicines. We made particular efforts to minimise criticism of our results in this regard. A note was therefore made of cases in which a specialist in the appropriate field had also made the diagnosis: 22.2% (cats) and 27.9% (dogs) of chronic cases were in this category. In any event, some conditions would not normally be appropriate for specialist referral. We have no reason to dispute the diagnosis of any of the conditions treated in this study. The presence of a clinical diagnosis by a veterinary specialist was not associated with any significant difference in the rate of +2/+3 outcomes in either cats or dogs.

The results make a clear case for a programme of targeted research in feline and canine homeopathy, including carefully designed RCTs in especially the most frequently treated conditions identified here. Such research would ascribe clearly established categories of diagnosis as well as objective evaluation of condition-specific outcomes at pre-determined time-points. Our new data confirm that individualised

prescribing is the usual approach to homeopathic management of both cats and dogs. This individualised approach to therapy is less amenable to explanatory, placebo-controlled, doubleblinded, trial design, 17,18 and the challenge to overcome the methodological difficulties must be met.<sup>19</sup> One practical response to the challenge has recently been piloted at the University of Bristol in research of homeopathy in atopic dermatitis in dogs, in which effects of homeopathic medicines were explored in a two-phase study design where only dogs that appeared to respond well to homeopathy in a initial noncontrolled phase went forward for investigation in a second, placebo-controlled, stage.<sup>20</sup> Another novel approach would be to research the efficacy of a given, well-indicated, homeopathic medicine for a specific condition (such as RRA in arthritis, as perhaps suggested by the present study's findings), where only patients matching that medicine's symptom picture would be randomised to verum or to placebo. Suitably designed pragmatic trials are also necessary to establish the effectiveness of individualised homeopathy in routine clinical practice. 21,22 Collaboration between homeopathic and conventional practitioners, as exemplified in the Bristol study, is key to pursuing high-quality research in homeopathic veterinary medicine.

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