(B) A total of 22 experiments were performed between 1991 and 2012, 15 by the initial team and 7 by altogether 5 independent researchers. In most of these experiments (the sole exception being two performed and reported by ourselves) a trend was found of T30x-animals being slower than W30x-animals. The differences in the individual subexperiments, each involving 60-100 animals per group, were mostly not statistically significant (p > 0.05). The pooled results of the initial team and those of the independent researchers did show significant differences (p < 0.01in either case). Pooled T30x values obtained by the initial team were 10.1% smaller than W30x values (100%) (p < 0.01 and d > 0.8), and pooled T30x values from the 5 independent researchers were 12.4% smaller (p < 0.01 and d > 0.8). Analogously, the number of animals entering the juvenile stage with reduced tail was smaller for T30x than for W30x.

Conclusion: A metamorphosis hormone diluted beyond Avogadro's limit using a process derived from homoeopathy produced a clear trend of metamorphosis inhibition. This was observed by 7 researchers from Austria, Germany, Switzerland and the Netherlands.

Amelioration of pain and distress in tail-ringed lambs using homeopathy

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Introduction: To reduce the incidence of blowfly strike in dirty fleece, lowland lambs in England usually have their tails docked at between 1 and 7 days old. A small and very tight rubber ring is applied to the tail 35 to 50 mm from the base of the tail, thereby constricting the blood supply. The distal part of the tail falls off 2 or 3 weeks afterwards. Whilst it is in the long term welfare interests of the sheep, this routine operation results in short term pain and discomfort for between 15 and 30 minutes. This experiment was conducted to see if homeopathy could be used to ameliorate the discomfort.

Methods: This triple blind controlled trial randomised 54 Dorset Down lambs into equal groups of both sexes. The verum group received a homeopathic complex of Aconite, Arnica and Hypericum, all at 200c, administered by mouth from a further diluted preparation in a spray bottle. The placebo group received an apparently similar preparation.

The behaviour of each lamb was recorded on a standardised form, every minute for 20 minutes. Every movement was categorised and counted using check marks, each time that type of movement occurred in each minute.

At the end of the study, the recording sheets were transferred onto a spreadsheet via a scoring system of 0 to 3, where 0 is "no stress" and 3 is "maximum stress". For example, standing, or lying down with head up would score 0 for "no stress"; whilst lying down on its side and thrash-

ing all four legs would score 3 for "maximum stress". Other categories of movement scored intermediate values.

Results: The spreadsheet for each lamb was scored for each movement and each minute. The scores for each minute were then totalled to give a score for the whole 20 minutes of study, to give the Area Under the Curve. This is an assessment of the total distress experienced by each of the lambs under study.

Frequency histograms were plotted for both groups; mean AUC scores for the verum group were 228.3 and for the placebo group were 320.7; giving an effect size score of 92.4 (c.i. 66.15 to 118.65; P<0.001). This amounts to a reduction in distress (reduced score) of 29% for the verum group.

Mean Distress Scores for each minute were also plotted for both groups. The peak distress for the verum lambs occurred about 3 minutes earlier than the placebo lambs and was 28% lower than the peak score for the placebo group. At the end of the 20 minute recording period, the final distress scores for the verum group were about 35% lower than the placebo group.

Conclusions: A reduction of approximately one third in total distress was achieved using homeopathic Aconite, Arnica and Hypericum 200c and is a practical and cost effective means of improving animal welfare on the farm.

Is homeopathic treatment as an effective intervention for children with a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD)?

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How to demonstrate Homeopathic effectiveness is an ongoing question. Pragmatic trials have high external validity, representing homeopathic treatment as it is practised in real life, and may provide a solution. Two studies provide examples.

A consecutive case series investigated whether homeopathic treatment is effective for children with ADHD. Twenty children received adjunctive homeopathic treatment and were compared with ten children not receiving homeopathic treatment at baseline and after 24 weeks, on DSMIV characteristics (Conner's Parent Rating Scale - CPRS) and a self-selected-item scale (Measure Your Own Medical Outcome Profile - MYMOP).

An analysis of variance (ANOVA) found a significant interaction between time and the treatment received. A long term analysis of treated children after one year found that they continued to improve, with half the participants registering improvement in their DSMIV scores of over 10 points. Different methodologies were explored to ascertain optimum treatment protocols, and CEASE

methodology proved especially effective for these children. It was found that remedies often needed repeating to retain effectiveness. This suggested obstacles to cure. CEASE proved effective at removing obstacles after which constitutional remedies needed repeating less often, and their effectiveness was enhanced. Despite the small sample size, this study suggests that homeopathic treatment is an effective intervention for children with ADHD. However limitations such as lack of randomisation, blinding and unequal sample sizes mean results have limited generalisability.

A Pragmatic Randomised Controlled Clinical Trial is being designed to enhance and develop the findings of the above Case Series and provide more powerful and robust evidence. The aim of the trial is to evaluate the comparative clinical and cost effectiveness of adjunctive treatment provided by homeopaths for children with a diagnosis of ADHD, in comparison to standard care alone.

Key elements of the design include the retention of the totality of homeopathic treatment; a control group receiving standard care; equal sample sizes of adequate power; random distribution of groups; groups representative of the ADHD population; homeopathic treatment undertaken by several homeopaths in several locations; evaluation of clinical and cost effectiveness using appropriate outcome measurements reflecting the requirements of stakeholders; and allowance of sufficient trial time to detect results. These studies into homeopathic effectiveness for ADHD are the first pragmatic studies comparing the totality of the homeopathic intervention with usual care. They build on the work of Frei (2005) and Lamont (1997) who demonstrated the effectiveness of Homeopathic remedies for children with ADHD; Jacobs (2005) who demonstrated the effectiveness of remedies and the clinical intervention. A systematic review recommended studies of 'homeopathy as it is practised by homeopaths ie pragmatic trials.

Cutting edge to clinical effectiveness: the implications of recent theoretical and research findings in homeopathy

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Much recent progress in research in homeopathy has been at polar ends of the spectrum: in theory and basic science and clinical effectiveness studies. I will review the implications for research in homeopathy.

'Weak quantum theory' hypotheses for homeopathy have been proposed by Walach and Milgrom. These hypothesise nonlocal action and 'entanglement' so that treatment effects occur in both treatment and control groups in randomised

controlled trials (RCTs). These hypotheses have been criticised for not suggesting an experimental test. Beauvais has applied a quantum-like statistical model to RCTs of homeopathy. This gives rise to a remarkable prediction: that the difference between between placebo and homeopathy groups vanishes in centralized blind trials due to 'smearing' (effects of homeopathy occurring in the placebo group). This could be overcome by in situ randomization/unblinding: the observables are measured and all operations from randomization to unblinding are performed locally in a defined order, without central supervision. Similarly Almirantis notes that if non-local factors are involved, there will be resistance to reproducibility, so effect sizes will be larger if control treatments were randomly selected homeopathic medicines, rather than blank, since this introduces uncertainty. These theories are testable and have important practical implications if verified.

Recent empirical findings in basic science include evidence on the role of nanoparticles of original substances, silica and gas. Bell's NPCAS model hypothesises that homeopathic medicines consist of nanoparticles, low level stressors cross-adapted to allostatic overload (allostasis is the physiological process of restoring homoeostasis, allostatic overload occurs when these mechanisms are overwhelmed). Implications for research include that outcomes should be multivariate and measured over time. These predictions are congruent with those made by nonlocal theories.

Nonlocal theories have not been tested, let alone verified. There are alternative explanations for the alleged lack of positive findings in RCTs of homeopathy. These include that there is nothing to explain. The results of meta-analyses are disputed and, as Mathie et al.'s recent bibliometric study showed, the literature has not been adequately searched: 30 eligible RCTs not listed by previous meta-analyses were found. Another possible explanation for false-negative results is the quality of homeopathy. Mathie has led the development of a method to evaluate the model validity of homeopathy in clinical trials.

There is a growing number of veterinary RCTs and animal experiments of relatively simple design with positive results. These include replication of the effects of highly dilute thyroxine on amphibian metamorphosis, nosodes for diarrhoea in piglets and an homeopathic complex in fish farming. These seem not to be in line with nonlocal hypotheses.

EPI-3 is a large scale comparative effectiveness study comparing GPs using homeopathy, mixed practice and conventional medicine in France. Upper respiratory tract infections, sleep disorders, anxiety and depression and musculoskeletal disorders were studied in terms of clinical benefit, medical care and medication consumption, adverse effects and loss of therapeutic opportunity. Patients seeking treatment from homeopathic GPs were similar to those attending conventional physicians. Homeopathy had advantages in at least one domain for each disease category.