Sir,

the study by Shang et al (Lancet 2005; 366: 726-32) does not support your headline of "the end of homoeopathy". The study itself, while attempting to eliminate false positive bias in randomised placebo-controlled homoeopathy trials (RCT) introduces bias by failing to assess for false negative bias. False-negative biases are omnipresent in RCT but we argue that they are more likely in homoeopathy.

- For example, in a paediatric RCT on respiratory infections, homoeopathy was provided versus placebo *in addition* to standard antibiotic treatment and tonsillectomy.[1] Homoeopathy had to prove *benefit additional* to conventional therapy, a difficult burden of proof. With homoeopathy being effective, control patients would need more antibiotics and surgery, and did so in this study. Such surplus of conventional therapies in control patients can easily compensate homoeopathy effects in verum patients and create false-negative results.
- False negatives are induced when the basic simile principle of homoeopathy is neglected and an identical single remedy given to all patients, making RCTs easier to perform. For example, a RCT on rhus tox. with individualized simile matching produced a positive result[2], a rhus tox. RCT neglecting simile turned out negative[3].
- Randomized trials have important limitations in complex treatment procedures that require particular skills[4]; homoeopathy, especially classical homoeopathy is highly skill dependent. Finding the correct homoeopathic simile depends on in-depth anamnesis in an atmosphere of trust, which is disrupted by randomization. Skilled practitioners with positive treatment experience are, for ethical reasons, less likely to participate in RCT.

Other false-negative factors are: drop-outs and non-compliers; contamination; informed consent; submissive answers; insensitive questionnaire, group assimilation, conditioning, cognitive interactions, etc. In one study, several can be present. Assessing trial quality according to randomisation, blinding and size does not weed out trials with false-negative bias: "Orthodoxy always invokes the danger of Type One errors to ensure the occurrence of Type Two errors!" (Eysenck, 1993). As Woods demonstrated, the logistics of large trials often need simplified protocols that easily lead to false-negative results.[5] Conditions necessary for quality homeopathy treatment, especially classical homeopathy are less likely to be provided in well randomized, well blinded and large trials. Unfortunately, the authors refused our requests to identify the decisive 14 "larger trials of higher reported methodological quality". This makes it impossible to assess if these larger trials allowed for optimal treatment conditions or if simplifications put homeopathy at disadvantage.

Shang et al interpreted asymmetric funnel plots as publication bias but this warrants further proof : the 1997 meta-analysis on homoeopathy (Linde et al) had dismissed publication bias after an extensive inquiry with manufacturers, researchers and practitioners. And concerning more pronounced between-trial heterogeneity in conventional medicine, its greater diversity of treatment methods also has to be taken in account.

In conclusion, this meta-analysis is far from confirmative and false-negative bias seems to have been the blind spot.

We declare that we have no conflict of interest.

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