Reviewer's report

Title: Method for appraising model validity of randomised controlled trials of homeopathic treatment: multi-rater concordance study

Version: 1 Date: 30 January 2012

Reviewer: Iris Bell

Reviewer's report:

Major Revisions None

Minor Essential Revisions None

Discretionary Revisions - see below

This paper addresses a major methodological issue in the design and assessment of homeopathic clinical trials, i.e., the model validity of the studies. The authors define the problem and question well and provide a well-written, systematic discussion of the rationale for their study. The methods and data are sound and provide an important advance in thinking about strengths and weaknesses of the existing homeopathic literature. The paper serves as a proof of principle methodological advance with 6 explicitly defined domains for assessing model validity of homeopathic research reports in addition to the more usual primary emphasis on internal validity used in medical research journals and meta-analyses.

The methodological approach described here will also have applicability for other fields of complementary and alternative medicine (CAM) research, notably acupuncture/traditional Chinese medicine and other whole systems of CAM. As such it is a significant contribution not only to improve homeopathic research reporting standards, but also to stimulate additional research in the broader area of CAM research.

The manuscript addresses the relevant standards for reporting and data management. In general, the discussion and conclusions are well-reasoned, supported by the data, and limitations are discussed. The title and abstract are appropriate for the subject matter of the paper.

As a homeopathic researcher, I am interested in seeing a small expansion of the discussion to address some questions on the application and limitations of the assessment domains studied.

These points are:

1. Could the authors speak more directly to the issue of how they dealt with or propose to deal with differing homeopathic schools of thought in applying the Domain I criteria. For this general non-homeopathic readership, the discussion
need not be lengthy, but it should address the question of different points of view in the field concerning the how to do homeopathic prescription of, for example, (a) combinations of multiple homeopathic remedies versus individualized homeopathic remedies; or (b) methods for remedy selection (e.g., purist classical homeopathy versus the Sensation Method, which also uses individualized remedy selection but utilizes a modified clinical assessment approach to choose the intervention. The intention of the intervention in the two examples mentioned above is homeopathic prescribing. Is this the criterion, as opposed to using a homeopathically-prepared remedy in a non-homeopathic prescribing manner (e.g., Lewith et al study)? Clarification on this point would help readers trying to apply the methodological evaluation methods to future studies.

Presumably, the Lewith et al paper appropriately failed the Domain I criterion because of the isopathic prescription of a specific remedy (dust mite) that most homeopaths would not use to treat chronic asthmatic patients for their chief medical complaint in the manner tested in the study. Isopathic prescribing of a is not homeopathic prescribing by definition, which makes this study easier to judge on this criterion.

2. Although the authors discuss the issue of grouping individuals as a function of a specified medical condition versus a characteristic pattern of signs and/or symptoms and leave the resolution of this point to future research, I would still prefer to see at least somewhat more discussion with literature citations pointing out the person-wide complexity and uniqueness of the clinical outcome picture in homeopathic prescribing, e.g., Oberbaum et al. Homeopathy 2005; 94:196-9; Bell et al J Altern Complement Med 2003; 9:39-50; Koithan et al . J Altern Complement Med 2007; 13:659-68.

Verhoef et al and colleagues, cited in the Background for this paper, have continued to pursue the question of how to look at outcomes in a human being during CAM treatment (upcoming special forthcoming issue of Forschende Komplementarmedizin, February, 2012). The perspective is that, to be true to CAM practice theories, it is not only the nature of the intervention, but also the nature of the patient outcomes that distinguishes homeopathy or acupuncture from biomedicine.

That is, the pattern of person-wide emergent outcomes is important, even central to the real-world clinical assessment of a patient’s progress. In homeopathic practice theory, a person is an indivisible complex adaptive system or network, whose nonlinear emergent outcomes cannot be parsed, in terms of real-world validity, into a static, single variable outcome (i.e., biomedical research designs).

This is not to reject the importance of biomedically-focused outcomes in choosing variables for study evaluation. Rather, it is to ask for attention to both (a) biomedical outcomes and (b) whole systems of CAM, whole-patient emergent outcome patterns as essential for the complete assessment of the model validity of a given study design. This will permit future evaluation of biomedical clinical trials not only by their own defined outcome measures, but also by whole systems of CAM (including homeopathy and acupuncture) real-world clinical
complex emergent outcomes criteria. Then studies can truly be evaluated side-by-side for relative strengths and weaknesses.

To summarize, while I agree with the pragmatic necessity of identifying a primary conventional outcome variable to map better onto the way biomedicine evaluates its treatments and permit comparison with conventional clinical trials, I believe that the topic of multiple, person-wide emergent outcomes needs greater acknowledgment in the Discussion of a paper on model validity of homeopathic clinical trials. This then becomes a logical point on which future studies on these challenging methodological issues can build.

Overall, I recommend that this paper be published after the authors make minor revisions to address the points raised here.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

My financial competing interest is that I am compensated as a homeopathic medical research consultant by Standard Homeopathic/Hyland's Inc, a U.S.-based manufacturer of homeopathic remedies. To my knowledge, there was no emphasis on products of any one homeopathic manufacturer over any other in the presentation of the papers discussed in this study. My own published research papers cited in this paper did not use this manufacturer's products.