Author’s response to reviews

Title: Homeopathy for Depression: a randomized, partially double-blind, placebo controlled, four armed study DEP-HOM

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Author’s response to reviews: see over
Dear Editor

We are very grateful for the thorough review process which helps to improve our manuscript. Our considerations (italics) follow each topic pointed out by the reviewer. Changes in the manuscript were highlighted in yellow.

With best wishes,

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Reviewer's report

Thank you for asking me to read this fascinating paper which I think addresses a vitally important issue in homeopathy: is it the consultation or the remedy that appears to produce the outcome or a combination of both?
I think in general this trial design is excellent but there are two major issues which leave me with some quite substantial concerns.

1. The type of homeopathy used. The majority of individuals who prescribe classical homeopathy in Western Europe would not tend to start by using LM or Q potencies. In the majority of instances, in my experience, the treatment of depression by homeopathy is based on the appropriate use of 30C, 200C and sometimes 1M potencies. This study appears to be based on one preliminary study carried out in Brazil and, as a consequence, does not reflect the reality of the day to day practice of homeopathy in Europe. Many of the clinical trials published within the field of homeopathy have adopted non-standardised methodology for conditions which are rarely treated by homeopaths in clinical practice. Depression and anxiety are commonly treated, but the authors would need to provide a much more convincing argument that the particular potencies they've chosen would be part of the standard management of anxiety and depression within a homeopathic context. The second issue relating to this is the very limited information given about the type of homeopathic encounter that will be used in this study. The introduction suggests that the Brazilian study assessed homeopathy as "a whole system". Without knowing very much about the consultation approaches that will be used (the authors state they don't want to compromise blinding), it is difficult to know whether real homeopathy will be delivered in a way that is generalisable to the practice of homeopathy in Europe.
Authors: As far as we know no systematic data on the homeopathic treatment strategies is available in Europe. Data from Germany (cohort study with 400 patients over 8 years Becker-Witt C, Lüdtke R, Weissshuhn TE, Willich SN. Diagnoses and treatment in homeopathic medical practice. Forsch Komplementarmed Klass Naturheilkd. 2004 Apr;11(2):98-103.) showed that 10% of the prescriptions are Q potencies. The treatment protocol of our current study was thoroughly developed in discussion with German homeopathic medical doctors (members of the German Homeopathic Doctors Association). It was also discussed with the department for homeopathy at the German drug agency and approved by them.

In addition the methodology was previously tested in a RCT carried out in Brazil (ref 17). It reflects a clinical-pharmaceutical protocol of classical homeopathy (ref. 21) developed by Hahnemann, which includes the standardized use of Q-potencies (Hahnemann CFS. Organon der Heilkunst: aude sapere. 6.Aufl., hrsg. u. mit Vorw. vers. von Richard Haehl, Leipzig, Schwuabe, 1921, Heidelberg, Haug, 1988 § 246, 248, 270). A sequence of ascending Q-potencies is easily reproducible and has already been successfully tested in RCTs for other conditions commonly treated by homeopaths, such as fibromyalgia (Bell IR et al. Improved clinical status in fibromyalgia patients treated with individualized homeopathic remedies versus placebo. Rheumatology 2004;43:577–82) or attention deficit hyperactivity disorder in Europe (ref. 31). Moreover, the type of homeopathy in DEP-HOM was defined as individualized (classic) in accordance with RedHot CONSORT extension for reporting randomized trials on homeopathy (please see ref. 29 and 30) and the analysis strategy was referenced (ref. 21). We also want to point out that this study is an experimental study with a focus on efficacy and not a pragmatic trial with a focus on effectiveness. We have stressed this matter also in the manuscript (see page 12 2nd paragraph).

2. The Homeopathic Consultation. The homeopathic consultation in itself is likely to be a vital component of the effectiveness of homeopathy in this condition. It is independently a very powerful therapeutic interaction.

Authors: We totally agree, that’s why we have decided to assess the impact of the consultation.

3. The nature and effect of the consultation. Because so little information is provided about the consultation itself, it is very difficult to know whether this will be a convincing generalisable and appropriate intervention. It appears that the homeopathic "diagnosis" will be made by one skilled physician based on answers to relatively standardised questionnaires. Have these questionnaires been piloted? How valid are they? Have other homeopaths looked at the questionnaires and are they generalisable to the very detailed nature of homeopathic practice within Europe?

Given that the homeopathic questionnaires and case histories will be vital, how convincing are the two different types of homeopathic consultation to the patient? Does belief influence outcome? Is there equipoise among both the patients and the practitioners with respect to this method of delivering homeopathy and if there is not, won't this give subtle messages to the patients which may serve to confound and bias the trial? This whole study revolves around the validity and generalisability of the consultation techniques used and yet we are given very little information about this absolutely vital component. Furthermore, the effect of the component and its credibility is poorly evaluated. There are no outcomes relating to empathy or credibility, simply to depression and general well-being.
Authors. The homeopath believes that the questionnaire works well to identify the homeopathic remedy. The content and structure of the questionnaire used in DEP-HOM follows Hahnemann’s case history instructions, with some additional questions stressing the symptoms of a depressive episode. The questionnaire was developed in consensus with members of the German Homeopathic Doctors Association and has been pretested. This information has been added to the manuscript. (see page 7 last paragraph).

Patients and rater are blinded to the two different types of homeopathic consultation and randomly assigned to them. That is why the manuscript and all study publications have little information about the consultation techniques. However, we agree that believes and expectation could influence the outcome if unblinding occurs. We evaluate the patients’ expectation at baseline and adjust for them in the analysis. However, the reviewer is right empathy would have been a good further measure.