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for time would have increased the scientific rigor of the study. Perhaps next time! Expectation is an important consideration and we are preparing a separate paper on this. Whether our patients may have known about the two different contextual conditions is indeed a concern. We cannot rule this out and this certainly is a potential confounder. Prospectively, we worried about this and one of the purposes of our concurrent nested qualitative study that selected 10% of patients for extensive interviews was to be able to tell all patients that some patients would be spending more time with a practitioner if they were selected for this 'extra' study. All patients knew about this qualitative study (it was written in the informed consent) and we assume that if anyone noticed differences in time they would assume it was because of the qualitative study. (The

results of this qualitative study will be reported in the future.) The informed consent said that patients in 'treatment' arms could expect to be randomly assigned to acupuncture or sham acupuncture and that in the 'treatment' arms they had a 50% chance of receiving genuine acupuncture. We agree that each patient had unique past experiences that could have conditioned them differently. (In fact, some in the 'limited' minimal treatment group commented in the qualitative study that they 'loved' the silent and meditative practitioner.) But we hope that our relatively large sample distributed these differences across the arms more or less equally, and our outcomes accurately reflect averages across many different kinds of people.

T Kaptchuk, Harvard Medical School, USA

Does acupuncture improve the results of *in vitro* fertilisation?

Manheimer E, Zhang G, Udoff L, Haramati A, Langenberg P, Berman BM, Bouter LM.

Effects of acupuncture on rates of pregnancy and live birth among women undergoing *in vitro* fertilisation: systematic review and meta-analysis.

BMJ 2008; **336**: 545-9.

Aim

To assess whether adjuvant acupuncture has an effect on the rates of pregnancy and live birth during *in vitro* fertilisation.

Data sources

Electronic searches in four databases complemented by hand-searching.

Study selection

Studies had to be randomised and use needle acupuncture compared to sham acupuncture or no adjuvant treatment.

Data extraction

Outcomes such as pregnancy, ongoing pregnancy or live birth were extracted by two reviewers or obtained from the authors of the primary publications. A meta-analysis of all randomised patients was performed.

Main results

Seven RCTs with 1366 patients were meta-analysed. Across all studies, acupuncture generated statistically and clinically superior results than control-interventions. Secondary analyses showed similar findings in RCTs comparing acupuncture with sham treatment or with no adjuvant treatment.

Authors' conclusion

'Current preliminary evidence suggests that acupuncture given with embryo transfer improves rates of pregnancy and live birth among women undergoing *in vitro* fertilisation.'

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Commentary

It is to the authors' credit to stress that the evidence is preliminary. The *BMJ* published two commentaries in parallel with this article. One pointed out that the review is technically good but not perfect.¹ The other stated that the effect size is larger than for any other procedure currently used to improve the success of *in vitro* fertilisation and that primary studies were sound.² It is with this latter point that I take issue.

Four of the seven RCTs made no attempt to control for placebo effects or to blind patients. Manheimer *et al.* state that the necessity to do so is 'arguable when the outcomes are entirely

objective'. On the face of it this makes sense but is it true in this case? What if the primary effect of acupuncture is a relaxation response which, in turn, increases pregnancy rates? Given the emotionally loaded clinical situation of trying to have a baby, this cannot be ruled out in my view. And if this were true, then surely we need to control for factors such as expectancy. Just three of the seven RCTs were sham-controlled trials, two of which failed to produce significant effects. This means the conclusions rely very much on one single study. Preliminary is therefore an apt term.

I have other concerns as well. Why is there no formal assessment of study quality? Perhaps because it would have demonstrated that, contrary to one commentator,² the primary data were flawed? Manheimer *et al.* stress in their abstract that 'there was little clinical heterogeneity'. If one bothers to read the primary studies, which is not easy because they are not part of the printed version of the article, one finds lots! Manheimer *et al.* also state that there should be little orientation bias as the financial stakes are not high in acupuncture. But what about the financial interests of the (mostly private) clinics which carry out *in vitro* fertilisation (and were responsible for virtually all the primary studies)? Or what about the quasi-religious beliefs of some acupuncturists?

In summary, this is a thought-provoking article but, before we recommend acupuncture for *in vitro* fertilisation, we should await the results of a large ongoing study from Denmark, as one of the commentators² wisely pointed out.

E Ernst, Peninsula Medical School,
Complementary Medicine, Exeter, UK

Conflict of interest None declared.

References

- 1 Clarke M. Commentary: Good but not perfect. *BMJ* 2008; **336**: 549.
- 2 Pinborg A, Loft A, Andersen AN. Acupuncture with *in vitro* fertilisation. *BMJ* 2008; **336**: 517-18.



Authors' reply

In *in vitro* fertilisation trials, the relevant outcomes (i.e. pregnancy and birth) are entirely objective, and therefore the need to use a sham control group to guard against patients' expectation effects is less important than in trials with subjective outcomes (e.g. pain). As Ernst has noted, it is possible that the effects of acupuncture on increasing pregnancy rates may be partially mediated through an expectation effect or by anxiety reduction, and our review offers little insight into the working mechanism of acupuncture.

However, the precise mechanism seems relatively unimportant from a clinical perspective. Furthermore, when a sham has effects that are part and parcel of the working mechanism of acupuncture, but without being a feasible alternative in clinical practice, you can learn little from sham-controlled trials. For clinically relevant conclusions, we need to compare realistic alternatives, like adjuvant acupuncture vs. no adjuvant to *in vitro* fertilisation. For the formal assessment of study quality, we used the internal and external validity criteria

recommended by the Cochrane Menstrual Disorders and Subfertility Group. This scale incorporates the criteria of the Jadad scale, and also includes many additional criteria. We described our quality assessment in the methods section and presented the assessments in extra Table C. We also included the full details of the characteristics of the included studies, as extra Table B. Both extra tables are available at <<http://www.bmj.com/cgi/content/full/336/7643/545>>. In terms of clinical heterogeneity, we noted that there were geographical differences in the nature of the *in vitro* fertilisation procedures typically used, and this probably explained the substantial heterogeneity of baseline rates. However, we pooled the studies' results because of the consistent effect of acupuncture across trials (with one exception), as well as because of the relative homogeneity of the acupuncture interventions, which is atypical for a non-pharmacological treatment.

E Manheimer et al., Center for Integrative Medicine,
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Acupuncture in migraine prevention - an underpowered clinical trial

Alexrim-Andrade J, Maciel-Junior JA, Carnè X, Severino Vasconcelos, Correa-Filho HR.

Acupuncture in migraine prevention: a randomized sham controlled study with 6-months posttreatment follow-up.

Clin J Pain 2008; **24**: 98-105.

Aim

To assess efficacy of acupuncture in migraine prophylaxis.

Design

RCT with two parallel arms.

Setting

Headache clinic of the State University of Campinas hospital in Brazil.

Participants

A total of 37 patients aged 18 to 50 years with migraine with and without aura diagnosed for at least a year; two to