

The report of the CACTUS study<sup>1</sup> and the accompanying editorial<sup>2</sup> are flawed by several biases and errors. The Editor's review gave the study an unjustified commendation by stating, 'A series of five-element acupuncture treatments has significant and sustained benefit in patients who frequently attend with medically unexplained symptoms'.<sup>3</sup> In fact, the flaws and biases are so many that we can expose only the most important ones: failure to consider clinical relevance and measurement precision, and failure to consider the risk of bias in unblinded pragmatic trials such as CACTUS.

The differences in outcome measures are small and imprecise and therefore unlikely to be relevant to patients. For example, the primary outcome measure in CACTUS was the Measure Yourself Medical Outcome Profile score at 26 weeks. For this outcome the difference was only -0.6 on a 7 point scale with a wide 95% confidence interval (-1.1 to 0.0). Had the graphs in Figure 2 shown the confidence intervals rather than the point estimates alone, it would have been inescapably obvious that, although some results are statistically significant, no results are clinically important.

When differences are statistically significant, the results cannot easily be explained by chance. However, this does not mean that they cannot easily be explained by bias, and the onus is on authors to justify assumptions that the risk of bias is small. Like many other advocates of acupuncture and integrative medicine, the authors and editorialists fail to understand two important limitations of unblinded pragmatic trials that rely on subjective outcome measures: first, that their results have a high potential for bias, and second, that the size of the bias effect is likely to be larger than effects specific to acupuncture.<sup>4</sup>

The purpose of having a control group to control for biases is undermined if there is no blinding and the control is not a true control, that is to say, similar in all aspects to the treatment group except for the treatment. In the CACTUS study, control group participants were not similar for, as the authors acknowledge, they were likely to have been unhappy about not receiving acupuncture. They were likely, therefore, to experience a negative placebo reaction, or as we have termed it, a 'frustrebo reaction'.<sup>5</sup> The measured placebo effect

will be the sum of the negative placebo or 'frustrebo effect' in the control group plus the positive placebo effect in the treatment group. To the unwary, the harm to the control group will appear as a benefit to the treatment group and the overall benefit of treatment (if any) will be exaggerated. We have explained this in greater detail elsewhere.<sup>5</sup> The statement that the statistician was blinded is irrelevant and serves no purpose other than to suggest some degree of objectivity.

It is a pity that the opportunity provided by the qualitative study to investigate likely causes of a negative placebo effect was lost. By restricting the qualitative study to those who had completed acupuncture, the chance was missed to capture the experience of those who had been denied it. A comparison between the test and control groups' feelings at 26 weeks would have been very informative.

It is convenient for advocates of complementary and alternative medicine that clinical relevance and the role of bias have been overlooked once again.

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## REFERENCES

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Paterson and colleagues do not provide any evidence for their claim that

acupuncture is effective for patients with multiple unexplained symptoms<sup>1</sup> for two main reasons. First, their study did not test acupuncture at all, and second, there were so many methodological flaws that no conclusions of any kind could reliably be drawn. Had no needling taken place, and patients in the intervention group simply been given the same amount of time talking to their physicians, could the authors state with any conviction, that the results would have been different? This question could be readily answered with a properly designed trial, that Paterson *et al* rejected in favour of their 'pragmatic' design.

But it gets worse. The study was stopped early (probably because of the slow recruitment that is reported in the paper), and at an interesting point. The figure showing the Measure Yourself Medical Outcome Profile scores for both treatment groups reveals that (a) effect sizes were very small, and (b) that the score for the intervention group oscillated above and below the line for the control group. Conveniently, the study stopped when the intervention score was higher than the control score.

The rationale for the study, as explained in the introduction, was that these patients consume substantial health care resources. Yet there was no effect of the intervention on these resources. For example, consultation rates were unchanged. Paterson *et al* try to justify their choice of study design as being more representative of clinical practice. But as there was no benefit to clinical practice, why do the study at all? Or at least, they should draw a conclusion that makes sense with regard to the data.

It is interesting to see that patients received explanations of 'five-element acupuncture'. Why were they thus misled as to how the body works, with misinformation that has no basis in science? Surely the days of paternalistic medicine are over? One has to wonder about a peer review system that allows such a flawed paper to be published. It does a disservice to science, and the damage is that it will be cited by opponents of evidence-based medicine, and even more patients will be misled.

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