Reviewer’s report

Title: Should we reconsider the routine use of placebo controls in clinical research?

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Reviewer: Frank Miller

Reviewer’s report:

This is a valuable paper that offers a balanced argument in favor of designing some randomized trials with usual care groups rather than placebo controls. The paper would benefit from a more clear critical focus on the underlying thesis that gives rise to the argument favoring usual care groups controls rather than placebo controls: the claim that a treatment is worthless if no better than a placebo control. It is the potential clinical relevance of treatments that work via the placebo effect that challenges this established thesis regarding the value of treatments and gives rise to the argument that in some cases treatments should be evaluated in comparison with usual care controls rather than placebo controls. It may be useful in this regard to discuss the evidence relating to the benefit of acupuncture for various pain conditions, such as low back pain. Some well-designed trials have demonstrated that traditional acupuncture is no better than a sham acupuncture intervention but that both are better than usual care. If superiority to a placebo control is the minimal standard of treatment value, then acupuncture should not be administered for low back pain. But, as the authors argue, this will deprive patients of the benefits of acupuncture, which has been shown to be superior to usual care. On the other hand, some additional limitations of validating treatments based on their propensity to promote placebo responses, rather than specific efficacy, deserve attention. If the benefits of acupuncture derive from positive expectations relating to a novel and exotic treatment ritual, it is possible that these benefits may diminish over time when acupuncture becomes a more familiar intervention. Thus there is reason to question the reliability and durability of treatment benefits derived from expectation alone, without benefit from the inherent pharmacological or physiological properties of the treatment.

A minor point relating to the text on p. 4. It is stated in the second paragraph that the placebo effect is "the tendency for a patient's condition to improve, not through a specific biological mechanism." However, we now know that there are a number of neurobiological mechanisms underlying placebo responses. Indeed, this very point is made in the following paragraph.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
No competing interests