My attention fell this week on the reporting of an article accepted for publication in one of the main journals in my field. According to the ABC , placebo treatments for pain can be effective even when patients know that it's a placebo.

The source for this report is the following article which is about to be published in the premier pain research journal *Pain* (as an interesting aside, note how the more authoritative a scientific journal is, the shorter its name is. I give you *Nature*, *Science*, *Cell*, *Circulation*, *Lung* to name just a few).

On closer examination, this publication becomes somewhat less newsworthy. It has all the classic hallmarks of a fluke result that is partly the result of the statistics used, and partly over-interpretation of fairly modest results. Given the authors claim they:

turn our understanding of the placebo effect on its head

I thought I had better take a look since this would be big news if true.

The study took place in Portugal, in a hospital pain clinic enrolling chronic back pain patients. The methodology was a small randomised controlled trial. Although double-blinding could have been possible and would have added substantially to the strength of the study design, for some reason there was a clear difference between the way the two groups were treated.

The group who received the open-label placebo treatment were given large orange capsules while the “treatment as usual” (TAU) group received nothing. Double- blinding could have been achieved by giving all the subjects placebo pills but having a separate researcher deliver the information about treatment allocation.

Instead, the placebo group were given a special briefing that was not given to the other group. To further compound the difference in treatment, the TAU group were told they would be given an opportunity to take the pills after the three weeks of the study period had been completed. Such a design is often used as a recruitment tool, but it inevitably enhances expectations and is part of a separate, distinct bias in research known as the Hawthorne effect .

There are a couple of other, smaller more technical flaws in the design but even if we decide not to quibble about those details, the results are far from impressive.

The authors report that despite their effective randomisation procedures, there was a difference in baseline pain score of 1.25 on a 10 point scale. This is not a small difference. The claimed effect of the placebo treatment was 1.5 points. Allowing that the treatment as usual group was already suffering slightly less pain on average, one would anticipate the gains from any treatment to be slightly smaller. That is exactly what was shown.

In assessing a new treatment for consideration in clinical use, the minimum effect size that will attract interest is at least 2.0 points on a 10 point scale.

The other outcome measure they used was the Roland-Morris Disability Questionnaire , which is a reliable and widely used research tool. The RMDQ is the most appropriate choice for research involving mild-to-moderate degrees of chronic pain so no complaints there.

However, there are some issues with the results which are not discussed in the paper. The RDMQ can be used with confidence to follow changes in disability only if the change in scores is greater than four points out of the 24 point scale . The reported changes in RDMQ scores were well below this threshold, hence this is at best an equivocal result and should be interpreted as such. One would be hoping for more than three weeks of improvement from a potentially unethical intervention. The study only followed patients to three weeks which is not even long enough for the well-documented

“placebo sag”
effect to kick in.

Small study size and short duration of follow-up tend to cause difficulties in the interpretation of potentially unexpected results because most unusual results disappear when the size of the study is increased. This is because the type of statistics used in small studies tend to flatter the intervention, an small differences between the study groups can be magnified.

Even if the results of this study were worthy of the breathless headlines, there still remains the issue that non-deceptive use of placebos is inherently unethical in my opinion because it medicalises the therapeutic transaction and entrenches a power disparity between patient and clinician.

In my experience, educated and empowered patients make good decisions about their treatment and experience less distress and better adjustment to their changed circumstances. The open-label placebo protocol used in this study was still deceptive as the use of Hawthorne effect was so powerful that most of the TAU group requested pill prescription after the three-week period and then demonstrated the same level of improvement as the intervention group in the study.

The only surprising thing to me about this finding was that the effect size was not large enough to be clinically relevant, given there was so much stacking of odds in their favour. So although the authors claim the protocol is not outright deceptive, it seems to me still very manipulative and exploits the ignorance of the patient about the lack of long-term efficacy that can be expected from placebo treatments.

So, once again, I will settle back into my armchair and keep reading my journals in pursuit of genuinely effective treatments that I can call upon for the benefit of my patients. I will not seek cheap shortcuts by manipulating my position of authority and instead will continue to try to educate and engage the people I look after so they become collaborators in their own long-term management.

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Read more http://theconversation.com/bubbles-of-nothing-are-not-something-lets-not-get-too-excited-about-non-deceptive-placebo-use-67460