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# Clinical Placebo Interventions Are Unethical, Unnecessary, and Unprofessional

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## INTRODUCTION

The American Medical Association Council on Ethical and Judicial Affairs (CEJA) has written a report on the clinical use of placebo interventions.[1] The CEJA position, adopted by the American Medical Association House of Delegates, is that placebo interventions are ethically acceptable if the patient is informed about the nature of the treatment, but that the information need not be such that the placebo intervention is clearly identified, nor is it necessary to seek specific consent before its administration. In the following I will argue that this position is not tenable.

## WHY AND HOW DO PHYSICIANS USE PLACEBO INTERVENTIONS?

Within the last five years, two large surveys of European or American clinicians have described how often, why, and how physicians treat patients with placebo interventions.[2] Our survey of 772 Danish physicians (with a response rate of 65 percent) found that 86 percent of general practitioners, and 54 percent of hospital-based physicians, said that they had used a placebo intervention at least once in the last year.[3] Half of the general practitioners (48 percent), and 10 percent of hospital-based physicians, said that they had used a placebo intervention more than 10 times within the last year. The most frequent reason given for placebo interventions was "to follow the wish of the patient and avoid a conflict." The most frequent placebo interventions were antibiotics (for example, for viral infections). Placebo interventions were considered ethically acceptable by 46 percent of the respondents.

The other survey, which included 466 academic physicians (with a response rate of 50 percent) at three Chicago-based medical schools, found that 45 percent of the respondents said that they had prescribed a placebo intervention within the last year, and 8 percent had used a placebo more than 10 times in the last year.[4] The most common reason for using placebo given was "to calm the patient" (18 percent). Other reasons included, for example, "unjustified demand for medication (15 percent)," and "to get the patient to stop complaining (6 percent)." In this survey also, the most typical placebo intervention was antibiotics. Half of the respondents (46 percent) thought a placebo intervention was permitted "when research supported its efficacy." The respondents reported that in 4 percent of the cases, patients were informed, "it is a placebo."

The CEJA statement mentions the possibility of "nocebo effects," and thereby probably thinks of placebo interventions as preparations containing no active drug, for example saline injections or lactose tablets, so-called "pure placebos." This is in conflict with the findings of these surveys, that the typical placebo is a drug, a so-called "impure placebo," in many cases an antibiotic. The ethical implication is that drugs have harmful effects. For example, antibiotics can result in serious allergic reactions for the individual being treated, and other harms; further, the unjustified use of antibiotics may cause the unnecessary development of bacterial resistance, creating potential problems for future patients who are in true need of antibiotics.

The central section of the CEJA report starts, "Physicians administer placebos because placebos might relieve the symptoms that cause distress to their patients." The statement thereby indicates that placebos typically are initiated for the benefit of patients. The report does state, in the middle of the text, and without a heading of its own, that it is not ethically acceptable to use placebo interventions "to serve the convenience of the physician rather than to promote the well-being of the patient," however, the prominent place given to the presentation of the ethically sound motive of helping the patient portrays the typical ethical situation as a dilemma between two valid ethical principles, that is, between promoting patients' well-being and respecting patients' autonomy. In contrast, the surveys find that placebo interventions typically are initiated for the "convenience" of the physician.

## CONVENIENCE PRESCRIPTIONS OF PLACEBO SHOULD BE AVOIDED

Convenience prescriptions of placebo interventions involve two quite different ethical scenarios that are not considered in the CEJA report. The first scenario involves a placebo treatment, for example "to get the patient to stop complaining," without informing the patient that the treatment is a placebo. Such a practice is clearly unethical, as it implies deception that is unbalanced by benevolence, and that carries the risk of harmful effects.

The second scenario involves disagreement about treatment. A patient wants a treatment that the physician thinks is unnecessary because there are no expected additional benefits. The physician clearly states this to the patient, who still wants the intervention. This is not a case of deception, but one of the physician's professional integrity being in conflict with the patient's wishes. Should a physician follow the wish of a patient and prescribe a placebo intervention? (Given that any treatment is a placebo when there is no expected additional benefit beyond that of the treatment ritual.) As stated, potential harmful effects to the individual patient — and, in the case of antibiotics, potential harm to future patients — speak strongly against this practice. Further, to prescribe an intervention only because the patient wants it implies a substantial transformation of the patient-provider relation. Ideally, a possibly imprudent treatment wish of a patient is checked by the physician's professional considerations, and a possibly imprudent treatment suggestion by a physician is checked by the patient's wishes. If a patient's wishes overrule professional considerations, the relation between patient and physician risks being transformed from one of mutual respect and dialogue to one resembling that between customer and shopkeeper.

Still, it is no simple task to decide when a treatment should be considered a placebo and when it is part of a defensive treatment strategy. In the case of antibiotics, one physician may conclude that a fever is viral and therefore consider antibiotics a placebo intervention. Another physician may conclude that the fever is *most likely* viral, but the risk of bacterial infection is not negligible, and will therefore not consider antibiotics to be a placebo intervention. Clearly, from a theoretical point of view, the two situations are very different, but from a practical perspective, they may merge in the inevitable clinical uncertainty. Whether an intervention is considered a placebo or an active treatment depends on a physician's gut feeling about the expected treatment benefit (beyond any effect of the treatment ritual). A physician's gut feeling may be very different from a patient's, and this tension represents a challenge to the physician-patient relationship. It is a challenge, however, that should be met with further dialogue and reconsiderations about the expected benefits and harms, and not by caving in and compromising professional integrity by prescribing ineffective and potentially harmful drugs.

## LITTLE EVIDENCE THAT PLACEBO INTERVENTIONS IN GENERAL HAVE CLINICALLY IMPORTANT EFFECTS

The CEJA report implicitly takes for granted that the effects of placebos are clinically relevant and universal. In the 1950s, it was commonly accepted that the effects of placebo were clinically relevant for many patients who experienced both subjective and objective improving outcomes in many clinical conditions.[5] However, this was a misconception based on flawed methodology. In most cases comparisons had been based on changes from baseline in a placebo group, and not on a more reliable comparison between a placebo and a no-treatment group.

Our review of 114 randomized clinical trials comparing placebo with no-treatment groups found no statistically significant effect on binary outcomes or on continuous-observer reported outcomes.[6] We found that patients who had received a placebo reported somewhat reduced subjective symptoms compared with untreated patients, but it was unclear to what extent this was due to the bias inherent in unblinded trials (for example, reporting bias) and to which extent the effect was real. We also found a statistically significant effect of placebo on pain, but the size of the improvement was modest, corresponding to 6 mm on a 100 mm visual analogue scale. This result was reproduced in 2004, when we updated the review with more than 50 additional trials.[7] Even assuming that an effect of placebo exists beyond the expected reporting bias, for example on pain, we know little about the situations that generate such an effect. Our predicament is that a few clinical trials show substantial effects, and many trials show no effects, or in some cases harmful effects, and there is no clear pattern that explains this variation.

Therefore, based on over 150 trials there is, on average, no evidence of clinically relevant effects of placebo interventions over a broad range of clinical conditions. Therefore, the main ethical argument for placebo prescriptions, that such interventions generally will benefit patients, is highly questionable.

## REPLACE PLACEBO TREATMENTS WITH EMPATHIC CONSULTATION STRATEGIES

An intervention, including a placebo intervention, is but one of many components of the patient-provider interaction. It is challenging to study the various components of patient-provider relationships and how the parties interact. Still, reviews indicate that the relation between a patient and a supportive person can have important effects on subjective and objective outcomes. One Cochrane review on the effect of a supportive person on labor concluded that it reduced the number of Caesarean sections, the number of women that needed analgesics, and the number of women with "unpleasant labours."[8] There is no need for placebo interventions. A better alternative is a consultation strategy involving dialogue, empathy, information about relevant facts, and joint decisions about diagnosis and treatments.

The CEJA mentions, "In some instances, it may be most appropriate to forego the use of placebos altogether." It would have been interesting to know CEJA's suggestion of why this is appropriate only in "some instances," and not always.

## THE CEJA POLICY ON PLACEBO OPENS THE GATE TO A DANGEROUSLY SLIPPERY AREA

The report states that clinical placebo interventions "may prove particularly valuable for conducting single patient controlled studies, known as *N*-of-1 trials." Such trials are a special version of randomized clinical trials. In this case an individual person with a reasonable stable chronic condition will engage in testing the effect of two or more treatments. Typically, the patient will be blinded, for example by using a placebo, and typically there will be several periods of treatments in a random order. However, *n*-of-one trials are rare, and their ethical problems are basically the ethical problems of clinical trials. Therefore, CEJA's emphasis on n-of-one trials in a report on the use of placebo in clinical practice is misplaced.

Still, the phrase "particularly valuable" has the implication that the report does not restrict use of placebo to *n*-of-one trials. Placebo intervention, according to the report, may be valuable (if not particularly so) outside *n*-of-one trials. One likely scenario envisaged by the CEJA could be a clinician in doubt about a treatment. He or she then discusses this with the patient, and prescribes various medications, including placebos, to try what works best, but without the formal design of the randomized sequences of *n*-of-one trial. However, such an approach is unethical. Without the bias-reducing techniques of randomization of treatment periods, and blinding procedures, informal experimentation has a very high risk of bias. Poorly conducted research is unethical, also when it comes to *n*-of-one trials. From the patient's perspective, it is preferable to either be referred to another physician with more knowledge about the clinical problem or to participate in a properly conducted *n*-of-one trial.

CEJA opens the gate to a dangerously slippery area when they recommend that the information provided to patients need not be such that the placebo intervention is clearly identified nor is it necessary to seek specific consent before its administration. The surveys indicate that physicians, when using placebo interventions, often inform their patients in a purposely vague manner, by stating "this is a substance that may help and will not hurt," or "it's a medication," or "this may help you but I am not sure how it works."[9] This practice is clearly unethical because patients are unaware that they will receive a placebo.

## CONCLUSION

The CEJA recommendations are problematic from a clinical, research, and ethical perspective. The recommendations do not address present placebo prescription practices, nor build on systematic reviews of randomized trials comparing placebo with no-treatment. A revised recommendation could include the following:

Clinical placebo interventions are unethical, unnecessary, and unprofessional. Placebo interventions are potentially harmful. First, placebo interventions are often drugs that involve a risk of harmful side-effects. Second, placebo interventions may damage patient-physician trust considerably, because they often involve deception and prescriptions for the convenience of the physician rather than for the well-being of the patient. Randomized trials generally find no effects, or modest subjective effects, of placebo interventions. Placebo interventions could, and should, be replaced by empathic consultation strategies.

## NOTES

1. N.A. Bostick et al., "Placebo Use in Clinical Practice: Report of the American Medical Association Council on Ethical and Judicial Affairs," in this issue of *JCE*.

2. A. Hróbjartsson and M. Norup, "The use of placebo interventions in medical practice — a national questionnaire survey of Danish clinicians," *Evaluation & the Health Professions* 26 (2003): 153-65; R. Sherman and J. Hickner, "Academic physicians use placebos in clinical practice and believe in the mind-body connection," *Journal of General Internal Medicine* 23 (2008): 7-10.

3. Hróbjartsson and Norup, see note 2 above.

4. Sherman and Hickner, see note 2 above. The study was published electronically in October 2007, which is considerably later than the drafting of the CEJA report. However, the point here is not the specific study cited, but that none of the several published studies of the clinical use of placebo was discussed in the report.

5. H.K. Beecher, "The powerful placebo," *Journal of the American Medical Association* 159 (1955): 1602-6.

6. A. Hróbjartsson and P.C. Gøtzsche, "Is the placebo powerless? An analysis of clinical trials comparing placebo treatment with no treatment," *New England Journal of Medicine* 344 (2001): 1594-602.

7. A. Hróbjartsson and P.C. Gøtzsche, “Is the placebo powerless? Update of a systematic review with 52 new randomised trials comparing placebo with no treatment,” *Journal of Internal Medicine* 256 (2004): 91-100.

8. E. Hodnett et al., “Continuous support for women during childbirth,” *Cochrane Database of Systematic Reviews* issue 3 (2007): article no. CD003766, *http://www.cochrane.org/reviews/en/ab003766.html.*

9. Sherman and Hickner, see note 2 above.