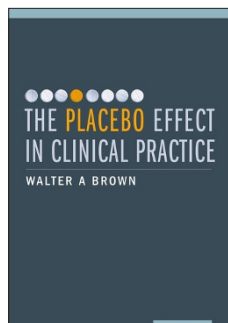


Rethinking placebos



The Placebo Effect in Clinical Practice

Walter A. Brown

Oxford University Press, 2012
188 pp., hardcover, \$45.00
ISBN: 0199933855

Reviewed by Irene Tracey

The placebo effect is the bane of clinical trial design because it causes many drug trials to fail. Nevertheless, researchers, clinicians and ethicists are increasingly interested in the use of placebos in clinical practice. That is why Walter Brown's *The Placebo Effect in Clinical Practice* is so timely. Extremely readable, this book is a must for anyone involved in biomedical research, clinical practice or the pharmaceutical industry, or even for the interested lay reader. Brown is a leading placebo researcher who, with facts drawn from the literature, challenges our attitudes about the placebo effect. He argues for the skilled use of placebos in clinical practice and suggests how to benefit from their scientifically proven effects.

Brown starts with a short history of placebos, reminding us that early medical practice was a catalog of placebo potions that worked because both physician and patient believed in their effectiveness. Early medical practice also established the link between patient and physician in the ritual of effective healing. Indeed, up until the mid-1950s, physicians published articles discussing how a placebo effect could be maximized in clinical practice—they understood that 'deception for good' was necessary to elicit patient improvement. Brown argues, provocatively, that a large number of current therapies, such as psychotherapies and surgical interventions, might essentially be placebos. Evidence of effectiveness over and above a placebo is unproven in many therapies owing to either ethical or practical difficulties.

Arguably, placebos have become the bad boys of modern medicine after publication of Henry Beecher's seminal paper in *JAMA* in 1955, which assessed the results of 15 studies with over a thousand patients who had been treated with placebos. Beecher concluded that because the placebo effect is so powerful, a drug must beat the placebo effect if it is to be approved: thus, the placebo-controlled trial was born. Brown correctly points out the irony that just when the effectiveness of placebo treatments was quantitatively proven, forcing this new design into clinical research, they stopped being used clinically as therapeutic agents.

Brown intelligently discusses how codes of ethics guiding research from 1980 onward affected the use of placebos in clinical practice and contributed to further misunderstandings about what placebo effects constitute. This chapter on ethics is especially welcome, as frequent

scrutiny of society's ethical position in the face of growing scientific knowledge is necessary, as evidenced by the American Medical Association's 2008 guidelines on the ethical use of placebo treatment in clinical practice.

Brown summarizes the findings from studies examining the placebo effect across a range of conditions. He offers insights about the variances in the magnitude of the placebo effect across diseases and suggests that there is no such thing as a placebo 'responder' or 'nonresponder'. This latter comment will stir debate, especially because trial designs using 'placebo run-ins' to identify placebo responders are popular. His argument is that 50 years of research have not identified clear trait or personality indicators predictive of the extent to which a subject will be a placebo responder—except in the case of children, who show large placebo responses. However, current research, though not discussed in the book, does suggest predictive factors might exist.

Remaining unclear is whether placebo effects influence disease mechanisms similarly to therapeutic interventions with identified efficacy or by indirectly influencing symptoms. We have the luxury of many objective methods in our modern armamentarium, such as neuroimaging, that have added to our current understanding of the placebo effect and helped overturn negative biases by showing that physiological effects do occur. It is too early to know whether placebos act in a mechanistically similar way to known therapies, but if they do, even for a subset of conditions, this challenges the ethics of not deploying a placebo manipulation in treatment regimens or in drug-dose reduction paradigms. Similarly, the lack of a no-treatment arm to allow for normal recovery in many trial designs prevents adequate distinction of the various mechanistic actions of drugs versus placebos, and Brown presents these issues skillfully.

Brown discusses the importance of the treatment environment for eliciting the placebo response well, and he makes a plea to rebrand the placebo effect as a "response to treatment situation." The idea that this situation promotes possible activation of brain circuits involved in driving well-being and perhaps a return to homeostasis harks back to ancient understandings of the importance of the patient-physician interaction. The author cleverly indicates how this interaction is degraded in our current climate, where appointment time windows are cut too short for meaningful interactions to occur.

Without getting bogged down by too much science, Brown presents enough to give the reader a grasp of the studies that have contributed to our understanding of how placebo effects are produced via expectation and conditioning. The relevance of expectation and its manipulation throughout a patient's journey is emphasized and is in keeping with research that highlights the role of expectation in influencing treatment outcomes. He also argues for reconsideration of expert exploitation of conditioned drug responses in clinical care.

Brown's book provides a calm account and discussion of the facts. Viewing placebos from many angles—scientific, ethical, clinical and historical—it is perhaps their sheer effectiveness that explains why they just will not go away. No longer a nuisance variable, placebos are here to stay, so we may as well use them.

COMPETING FINANCIAL INTERESTS

The author declares no competing financial interests.

Irene Tracey is at the University of Oxford, Oxford, UK.
e-mail: irene.tracey@ndcn.ox.ac.uk