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"Can You Handle the Truth?"

"Wiley Encyclopedia of Clinical Trials"

Ralph B. D'Agostino, Lisa Sullivan, and Joseph Massaro, editors, 2008, 2,466 pages (4 volumes), Wiley, \$1,400

Review by Norman M. Goldfarb

"Wiley Encyclopedia of Clinical Trials" weighs in at 11 pounds of concentrated clinical research knowledge. Three editors-in-chief, a 17-member editorial review board, and 338 authors produced 390 articles, averaging 5.6 pages length.

This book has been selected for
[The First Clinical Research Bookshelf](#)
Essential reading for clinical research professionals

A sample section of the index demonstrates the breadth of the content and its emphasis on biostatistics:

- Clinical Data Coordination
- Clinical Data Management
- Clinical Hold Decision
- Clinical Significance
- Clinical Trial Misconduct
- Clinical Trials to Support Prescription to Over-the-counter Switches
- Cluster Randomization
- Cochrane Collaboration
- Code of Federal Regulations (CFR)
- Coherence in Phase I Clinical Trials
- Cohort vs. Repeated
- Cross-Sectional Survey Designs
- Collinearity
- Combination Therapy
- Committee for Medicinal Product for Human Use (CHMP)
- Common Technical Document (CTD)
- Community-Based Breast and
- Cervical Cancer Control
- Community Intervention Trial for Smoking Cessation (COMMIT)
- Compliance and Survival Analysis
- Composite Endpoints in Clinical Trials
- Computer-Assisted Data Collection
- Conditional Power in Clinical Trial Monitoring
- Confidence Interval
- Confidence Intervals and Regions
- Confirmatory Trials
- Confounding

The encyclopedia includes material for non-technical people, but most of the articles are scholarly, with extensive references. The following section on the magnitude of the placebo effect from a six-page article on placebos illustrates the style of content and writing:

For decades, the placebo response has been assumed to be similar across disease categories at approximately 35% improvement from baseline (3). This figure has been applied equally to the proportion of patients improving and to the degree of improvement per patient per outcome. More recently, doubt has been cast on the constant placebo response, as evidence accumulates that both the true and perceived placebo effects are variable (15,36,55). A review of 75 trials of antidepressant medications revealed that the placebo response rate varied from 12.5 to 51.8% and had increased over time (55). A recent systematic review of randomized trials with placebo and no-treatment arms concluded that there was evidence of a mild true placebo effect for some subjective outcomes (e.g. pain and anxiety) but not for more objective outcomes (blood pressure, weight loss, asthma outcomes) (23). For example, placebo was associated with a reduction in pain by a mean of 0.65 cm on a 10 cm visual analog scale, as compared with no treatment. The authors measured the difference in outcomes between the two arms at the end of the treatment period, rather than the change in outcomes from baseline, thus attempting to control for the nonspecific effects and determine the true placebo effect (22). Their concluding caution against the use of the placebo and its effects for therapeutic purposes outside of a controlled clinical trial raised a storm of criticism. Although the validity of the findings were questioned, in terms of widely varying populations and diseases, heterogeneity and low statistical power (1,46), wrong choice of placebo (27), and contamination of the “no-treatment” arms (14), in our opinion, it is really the generalizability of the findings that is in question. Within randomized controlled trials, where patients acknowledge by their consent that they know they may not receive an active treatment, the perceived (total) placebo effect may be more muted than in clinical practice. Furthermore, even within randomized trials, unblinding can occur and bias clinician and patient — a situation bound to happen with a no-treatment arm. Finally, and most important, a finding that placebo therapies and no-treatment arms do not differ does not negate the possibility that a true placebo effect occurred (and occurred equally) in both groups.

It is important to keep in mind that placebos are not risk-free. Placebos may be harmful if they delay access to effective therapy for the disease under investigation, if their nonspecific symptomatic effects mask a condition that has effective treatment, or via direct nocebo effect (1). Where placebos are used without patient consent, any revelation of the deception may seriously undermine patient–physician relationship, which is itself a powerful source of “placebo effect.”

The book is available in bookstores. An online version is available at <http://mrw.interscience.wiley.com/emrw/9780471462422/home/>.

Reviewer

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