“Designing Clinical Research, 4th Edition”


Review by Norman M. Goldfarb

“Designing Clinical Research, 4th Edition” is a practical, common sense guide for research investigators, as well as other research professionals who want to understand how their work fits into the big picture. The book covers a broad range of human subject research—translational, clinical trial, patient-oriented, epidemiological, behavioral and health services—from fundamental concepts to functional ethics to funding proposals.

Research questions should meet the “FINER” criteria: feasible, interesting, novel, ethical and relevant. Once the question is asked, the important criterion becomes good design, the main focus of this book. These criteria seem obvious, but apparently not to the authors of thousands of misconceived studies that will be published this year. In the absence of evidence to the contrary, we will assume that none of them has read this book.

A more-or-less random selection from the book yields this explanation of potential bias due to conditioning on a shared effect:

The bias caused by conditioning on a shared effect is kind of tricky, and it is sometimes skipped in introductory textbooks because most explanations of it use abstract diagrams and notation. By contrast, we will first give a few examples of how it might occur and then try to explain what the name means.

Consider a study of people who have lost at least 15 pounds in the previous year. An investigator finds that the subjects who have been dieting have a lower risk of cancer than those who have not been dieting. Do you think dieting prevented cancer in these subjects?

If you stop and think, you’ll probably answer no, because cancer also causes weight loss. You can imagine that if someone loses weight for no apparent reason it is much more likely to signify a cancer than if someone loses weight while dieting. Among people who have lost weight, if the weight loss was not caused by dieting, it is more likely to have been caused by something more ominous. The investigators created an inverse association between dieting and cancer by conditioning on (restricting attention to) a shared effect (weight loss, which is caused by both dieting and cancer).

Here's another example. Among low birth weight babies, those whose mothers smoked during pregnancy have lower infant mortality than those whose mothers did not smoke. Should we encourage more mothers to smoke during pregnancy? Definitely not! The reason for this observation is that smoking causes low birth weight, but so do other things, especially prematurity. So among low birth weight babies, if the low birth weight was not caused by smoking, it is more likely to have been caused by prematurity. The investigators created an inverse association between smoking and prematurity (and its associated mortality risk) by conditioning...
on (restricting attention to) a shared effect (low birth weight, which is caused by both smoking and prematurity).

Now the phrase "conditioning on a shared effect" makes sense. Conditioning is an epidemiologic term that means looking at associations between predictor and outcome variables "conditioned on" (i.e., at specified levels of) some attribute. A shared effect refers to an attribute (like losing weight or being a low birth weight baby) that has several causes. Bias due to conditioning on a shared effect can occur if the investigator treats something caused by the risk factor being studied as an inclusion criterion, a matching variable, or a possible confounding variable.

The few formulae in the book are confined to the chapter on sample size and power. Statistical analysis and publication are not covered.

The book consists of 19 chapters:

- Getting Started: The Anatomy and Physiology of Clinical Research
- Conceiving the Research Question and Developing the Study Plan
- Choosing the Study Subjects: Specification, Sampling and Recruitment
- Planning the Measurements: Precision, Accuracy and Validity
- Getting Ready to Estimate Sample Size: Hypotheses and Underlying Principles
- Estimating Sample Size and Power: Applications and Examples
- Designing Cross-Sectional and Cohort Studies
- Designing Case-Control Studies
- Enhancing Causal Inference in Observational Studies
- Designing a Randomized Blinded Trial
- Alternative Clinical Trial Designs and Implementation Issues
- Designing Studies of Medical Tests
- Utilizing Existing Data
- Addressing Ethical Issues
- Designing Questionnaires, Interviews and Online Surveys
- Data Management
- Implementing the Study and Quality Control
- Community and International Studies
- Writing a Proposal for Funding Research

The book is available in bookstores.

**Reviewer**

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