Designing Clinical Research

FOURTH EDITION

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To our families and our students
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Introduction

This fourth edition of Designing Clinical Research (DCR) marks the 25th anniversary of the publication of our first edition. It has become the most widely used textbook of its kind, with more than 130,000 copies sold and foreign language editions produced in Spanish, Portuguese, Arabic, Chinese, Korean, and Japanese. We designed it as a manual for clinical research in all its flavors: clinical trials, observational epidemiology, translational science, patient-oriented research, behavioral science, and health services research. We used epidemiologic terms and principles, presented advanced conceptual material in a practical and reader-friendly way, and suggested common sense approaches to the many judgments involved in designing a study.

Many of our readers are physicians, nurses, pharmacists, and other health scientists who, as trainees and junior faculty, are developing careers in clinical research and use this book as a guide in designing and carrying out their studies. Many others are clinicians in residency programs and pre-doctoral students in professional schools—medicine, nursing, pharmacy, and public health among others—who use DCR to help them become discerning readers with a grasp of the strengths and limitations of the research studies that inform evidence-based clinical practice. A third audience consists of undergraduate students preparing to apply to these schools who are interested in looking ahead at the world of clinical research.

What’s new in the fourth edition? The most visible innovation is color, which, in addition to improving the esthetics, will speed comprehension of the color-coded components. A larger innovation that accompanies each purchase of the paperback text is an interactive digital experience powered by Inkling®, viewable through a browser or as a download to tablet or smartphone. Its features include rapid index-based search options that link to a newly created glossary; bookmarking, highlighting, and annotating capability; cross-linking of relevant content; the ability to cut-and-paste figures or text into PowerPoint presentations; and live Internet links to jump instantly from citations to articles on PubMed, and to Google topics.

The substantive revisions to the fourth edition include updated and tightened text, figures, and tables in every chapter; many new examples and references; and new sections covering recent advances in the field. For example:

• The chapters on observational studies have been reorganized with an entire chapter now devoted to various case–control designs, including the incidence-density approach for addressing changes in risk factor levels and differences in follow-up time.
• The chapters on clinical trials have an expanded section on the non-inferiority trials that have become popular in comparative effectiveness research, and they address subgroup analysis and effect modification more fully.
• The chapter on studying medical tests has a new section on the growing practice of developing clinical prediction rules.
• The chapter on utilizing existing data sets emphasizes attractive options for beginning investigators to publish rapidly and inexpensively.
• The chapter on research ethics is updated to reflect current policy on whole genome sequencing and other topics, with new cases that illustrate the resolution of ethical dilemmas in clinical research.
The chapter on data management has been extensively updated with the latest Web-based approaches.

The chapter on getting funded has strategies for addressing the new NIH grant-writing requirements, as well as updates on funding by foundation and corporate sponsors.

The fourth edition is accompanied by an upgraded DCR website at www.epibiostat.ucsf.edu/dcr/ that contains materials for teaching DCR, including links to a detailed syllabus for the 4- and 7-week DCR workshops that we present to 300 trainees each year at UCSF. There are also instructor’s notes for the workshops that faculty who teach this material will find useful, and links to our Training In Clinical Research (TICR) master’s degree program at UCSF, with more than 30 other courses and their materials. In addition, there are useful tools for investigators, including an excellent interactive sample size calculator.

Many things have not changed in the fourth edition. It is still a simple book that leaves out unnecessary technicalities and invites the investigator to focus on the important things: how to find a good research question and how to plan an efficient, effective, ethical design. The chapters on estimating sample size continue to demystify the process and enable readers with minimal training in statistics to make these calculations themselves, thoughtfully, and without needing to wrestle with formulas. The book still works best when combined with the essential ingredient of one or more long-term mentors. It still does not address the important areas of how to analyze, present, and publish the findings of clinical research—topics that our readers can pursue with other books (e.g., 1–4). And we still do use the feminine pronoun in the first half of the book, masculine in the second, the goal (besides avoiding the passive tense) being to symbolically empower clinical investigators of both genders.

The process of becoming an independent clinical scientist can be challenging, especially getting over the hump of acquiring a substantial grant for the first time. But it is gratifying that many of our former trainees who used this book have achieved this goal, discovered that they like doing research, and settled into a great career. For those with inquiring minds, the pursuit of truth can become a lifelong fascination. For perfectionists and craftsmen, there are endless challenges in creating elegant studies that conclusively answer questions, large and small, at an affordable cost in time and money. Investigators who enjoy teamwork will develop rewarding relationships with colleagues, staff, and students, as well as friendships with collaborators working in the same field in distant places. And for those with the ambition to make a lasting contribution to society, there is the prospect that with skill and tenacity they will participate in the incremental advances in clinical and public health practice that is the natural order of our science.

REFERENCES

We are grateful to the Andrew W. Mellon Foundation for bringing the five of us together 30 years ago to begin the five-year journey of developing the teaching materials that became the first edition; to our publisher for steadily inviting a fourth edition until resistance became futile, and for providing exceptionally talented and supportive professionals to help us put it together; to our families for their patient support as we labored over this opus; to many colleagues at UCSF and beyond, whose ideas have influenced ours; to our students over the years, whose accomplishments have been fun to watch and stimulating to our thinking; and to our readers who have put this book to use.