
Principles of Research Methodology

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Editors

Principles of Research Methodology

A Guide for Clinical Investigators

Foreword by Stephen E. Epstein

 Springer

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Foreword

This superb book on research philosophy and methodology that Drs. Phyllis Supino and Jeffrey Borer have written and edited came out of an experience common to most of us involved in training investigators beginning their research careers. How do you teach these investigators the mostly unwritten ways of an area as complex as medical research? How do you help the research neophyte develop into a creative and reliable researcher? For me and my associates in the Cardiology Branch of the NIH (of which Dr. Borer was one) in the 1970s and 1980s, the teaching process was mostly based on an apprenticeship model, with learning coming in the actual doing of the research. This time-honored approach led to the development, in many research centers, of a cadre of superb researchers—but it was hard to master and the results were necessarily inconsistent, with many young investigators going down wrong paths.

Drs. Supino and Borer's book represents a unique collaboration between an accomplished educator specializing in research methodology and a prominent physician-scientist. Drs. Supino and Borer began their collaboration more than 20 years ago at Cornell University Medical College, continuing their work together in what became the Howard Gilman Institute for Valvular Heart Diseases. The Institute, of which Dr. Borer is the Director, now is located at the State University of New York Downstate Medical Center. Working within the context of a research institute housed within a medical school, Dr. Borer soon discovered that most of the fellows coming into his program had no formal research training and scant knowledge of research methodology. Prior to joining the Institute, Dr. Supino had been conducting continuing education in research methodology for scientists and health professionals since late 1970's. When Dr. Supino joined the Institute in 1990, she applied her accumulated expertise in this field to develop a curriculum and lead a comprehensive course providing formal training in research methodology for Dr. Borer's fellows and others at the institution. This curriculum and course, developed in partnership with Dr. Borer, turned out to be our good fortune. During the ensuing 20+ years Drs. Supino and Borer gradually developed the pedagogical framework for writing what is one of the best books in the field.

This book provides in depth chapters containing information critical to creating good research—from the kind of mind-set that generates valuable research questions to study design, to exploring a variety of online data

bases, to the elements making for compelling research grants and papers, and to the wonderfully informing chapter on the history of the application of ethics to medical research. There also is a valuable chapter on statistical considerations and a fascinating discussion on the origins and elements of hypothesis generation.

It's also important to emphasize that this superb text is not only for the new investigator, but for experienced investigators as well. This results from the fact that Drs. Supino, Borer, and their coauthors write their chapters in ways that are not only easily accessible to the new investigator, but at the same time are sufficiently sophisticated so that the seasoned investigator will profit.

As an example, I particularly enjoyed the first chapter, written by Dr. Supino, which provides some down to earth examples of, in essence, why there should be a clearly defined primary endpoint in clinical investigations. As I was reading her chapter, I realized I had forgotten the "why" of this requirement, and that I was just taking the requirement for granted—a situation that could make investigators vulnerable to dismissing its importance. In this regard, over the years I've found it not uncommon for investigators, who find that the efficacy of the intervention they're studying significantly improves one or another secondary endpoints but not the primary endpoint, to freely attack this "requirement" and argue they've proven the efficacy of their intervention. But Dr. Supino reminds us what good science is by providing an elegantly simple example of the marksman who boasts his skills after interpreting the results of his shooting a gun at a piece of paper hung on the side of a barn. The marksman, it turns out, does not prospectively define the "bull's eye". Rather, after multiple bullets are fired at the piece of paper, he inspects the bullet hole-riddled paper, sees the random bullet hole patterns, and then draws a circle (bull's eye) around a group of holes that by chance have fallen into a tight cluster. The post hoc definition of the bull's eye (i.e., now the "primary endpoint") speaks (unjustifiably) to the marksman's skill. By this simple anecdote, Dr. Supino makes the critical importance of prospectively defining the primary endpoint exquisitely clear.

A foreword is no place to provide extensive details of what a book contains. I'll therefore limit myself and just enthusiastically say this first chapter I read is representative of the high quality of the chapters to come. Drs. Supino and Borer have used the many years they have developed their course extraordinarily well—they and their outstanding coauthors have produced a book that is well written, beautifully edited, and contains wisdom and insight. It is a book, whether reading it in its entirety or perusing individual chapters, that presents the reader with a superb learning experience. The authors have certainly hit the bull's eye.

Washington, DC, USA

Stephen E. Epstein, MD

Preface

This book has been written to aid medical students, physicians, and other health professionals as they probe the increasingly complex and varied medical/scientific literature for knowledge to improve patient care and search for guidance in the conduct of their own research. It also is intended for basic scientists involved in translational research who wish to better understand the unique challenges and demands of clinical research and, thus, become more successful members of interdisciplinary medical research teams.

The book is based largely on a lecture series on research methodology, with particular emphasis on issues affecting clinical research, that the editors designed and have offered for 21 years to more than 1,000 members of the academic medical communities of Weill Cornell Medical College and the State University of New York (SUNY) Downstate Medical Center, both located in New York City. The book spans the entire research process, beginning with the conception of the research problem to publication of findings.

The need for such a book has become increasingly clear to us during many years of conducting a program of training and research in cardiovascular diseases and in our general teaching of research methodology to students, trainees, and postgraduate clinical physicians and researchers. Though agreement on the fundamental principles of scientific research has existed for more than a century, the application of these principles has changed over time. The precision required in defining study populations and in detailing methodologies (and their deficiencies) is continually increasing. In addition, a bewildering arsenal of statistical tools has developed (and continues to grow) to identify and define the magnitude and consistency of relationships. Simultaneously, acceptable formats for communicating scientific data have changed in response to parallel changes in the world at large, and under the pressure of an “information explosion” which mandates succinctness and clarity.

Despite these demands, there are few books, if any, that comprehensively and concisely present these concepts in a manner that is relevant and comprehensible to a broad professional medical community. This text is designed to resolve this deficiency by combining theory and practical application to familiarize the reader with the logic of research design and hypothesis construction, the importance of research planning, the ethical basis of human subjects research, the basics of writing a clinical protocol, the logic and techniques of data generation and management, and the fundamentals and implications of various sampling

techniques and alternative statistical methodologies. This book also aims to offer guidance for assembling and interpreting results, writing scientific papers, and publishing studies.

The book's 13 chapters emphasize the role and structure of the scientific hypothesis (reinforced throughout the various chapters) in informing methods and in guiding data interpretation. Chapter 1 describes the general characteristics of research and differentiates among various types of research; it also summarizes the steps typically utilized in the hypothesis-testing (hypothetico-deductive) method and underscores the importance of proper planning. Chapter 2 reviews the origins of clinical research problems and the types of questions that are commonly asked in clinical investigations; it also identifies the characteristics of well-conceived research problems and explains the role of the literature search in research problem development. Chapter 3 introduces the reader to various modes of logical inference utilized for hypothesis generation, describes the characteristics of well-designed research hypotheses, distinguishes among various types of hypotheses, and provides guidelines for constructing them. Chapter 4 takes the reader through classic epidemiological (observational) methods, including cohort, case-control, and cross-sectional designs, and describes their respective advantages and limitations. Chapter 5 discusses the meaning of internal and external validity in the context of studies that aim to examine the effects of purposively applied interventions, identifies the most important sources of bias in these types of studies, and presents a variety of alternative study designs that can be used to evaluate interventions, together with their respective strengths and weaknesses for controlling each of the identified biases. Chapter 6 defines and describes the purpose of the clinical trial and provides in-depth guidelines for writing the clinical protocol that governs its conduct. Chapter 7 describes methodologies used for data capture and management in clinical trials and reviews associated regulatory requirements. Chapter 8 explains the steps involved in designing, implementing, and evaluating questionnaires and interviews that seek to obtain self-reported information. Chapter 9 reviews the pros and cons of systematic reviews and meta-analyses for generating secondary data by synthesizing evidence from previously conducted studies, and discusses methods for locating, evaluating, and writing them. Chapter 10 describes the various methods by which subjects can be sampled and the implications of these methods for drawing conclusions from clinical research findings. Chapter 11 introduces the reader to fundamental statistical principles used in biomedical research and describes the basis of determination of sample size and definition of statistical power. Chapter 12 describes the ethical basis of human subjects research, identifies areas of greatest concern to institutional review boards, and outlines the basic responsibilities of investigators towards their subjects. Finally, Chapter 13 provides practical guidance on how to write a publishable scientific paper.

The authors of this book include prominent medical scientists and methodologists who have extensive personal experience in biomedical investiga-

tion and in teaching various key aspects of research methodology to medical students, physicians, and other health professionals. They have endeavored to integrate theory and examples to promote concept acquisition and to employ language that will be clear and useful for a general medical audience. We hope that this text will serve as a helpful resource for those individuals for whom performing or understanding the process of research is important.

Brooklyn, NY, USA

Phyllis G. Supino
Jeffrey S. Borer

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