

Peter D. Fabricant

Practical Clinical Research Design and Application

A Primer for Physicians, Surgeons,
and Clinical Healthcare Professionals



Springer

Practical Clinical Research Design and Application

Peter D. Fabricant

Practical Clinical Research Design and Application

A Primer for Physicians, Surgeons,
and Clinical Healthcare Professionals

 Springer

Peter D. Fabricant, MD, MPH
Associate Professor of Orthopedic Surgery
Hospital for Special Surgery
New York, NY, USA

ISBN 978-3-031-58379-7 ISBN 978-3-031-58380-3 (eBook)
<https://doi.org/10.1007/978-3-031-58380-3>

© The Editor(s) (if applicable) and The Author(s), under exclusive license to Springer Nature Switzerland AG 2024

This work is subject to copyright. All rights are solely and exclusively licensed by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

If disposing of this product, please recycle the paper

*To Son and Avery, my constant source of
support and encouragement in every way.*

Preface

The practice of medicine and surgery requires dedication to lifelong learning. As such, every practicing physician, surgeon, advanced practice provider, and allied health professional interacts regularly with peer-reviewed literature, either while creating it or consuming it. Despite the countless hours over many years spent in formal clinical training, many clinicians and clinician-authors lack advanced training or a working nuanced knowledge of research methodology and study design. Institutions have responded to this gap by reinforcing their ranks with statistical and methodological support in the form of data analysts, epidemiologists, and biostatisticians. However, clinicians are too often unable to “talk the methodological talk” to guide them. This ultimately results in a stark disconnect between clinically relevant aspects of research (i.e., what clinicians want to study) and appropriate study design (i.e., choosing and executing the correct methodology to answer the question).

I wrote this book after realizing the need for a concise, readable, and practical guide for clinicians to read and reference. Although many textbooks will “get into the weeds” with statistical and epidemiological theory and equations, they are not easily digestible by trainees and practicing clinicians who want pragmatic knowledge of this content in order to design their own studies or enhance their understanding of the medical literature.

It is my hope that this book can serve as a standalone text “written by a clinician, for clinicians,” but from the perspective of someone with formal training in research methodology, biostatistics, and epidemiology.

New York, NY, USA

Peter D. Fabricant, MD, MPH

Acknowledgments

I would like to sincerely thank Dr. Shevaun Doyle who inspired the idea for this book and spent many hours reviewing and editing the work, and Dr. Rob Rozbruch for helping formulate my ideas into a formal book proposal.

My wife, Dr. Son McLaren, deserves special recognition for her thoughtful and thorough editorial critique as well as serving as a friendly debate partner for much of this book's contents.

I would also like to thank my research assistants during this time, Preston Gross and Ruthie Jones, for their help with manuscript preparation and figure production.

Finally, I would like to acknowledge my mentors, colleagues, and Hospital for Special Surgery, all of whom have created an environment in which to build a thriving clinical practice while meaningfully contributing to research and education.

Contents

Part I Foundational Basics

1	Descriptive Statistics	3
	Introduction	3
	Types of Descriptive Statistics	3
	Measures of Central Tendency	3
	Measures of Variability	4
	Measures of Distribution	6
	Importance of Descriptive Statistics	8
	Conclusion	9
	Reference	9
2	Comparative Statistics: Categorical Data	11
	Introduction	11
	What Is Categorical Data?	11
	How Is Categorical Data Best Graphically Represented?	12
	Bivariable Statistics for Categorical Data	13
	Calculating Expected Cell Counts	13
	Post Hoc Pairwise Analyses	14
	Multivariable Statistics for Categorical Data: Logistic Regression	14
	Conclusion	16
	References	16
3	Comparative Statistics: Continuous Data	17
	Introduction	17
	What Is Continuous Data?	17
	How Is Continuous Data Best Graphically Represented?	18
	Bivariable Statistics for Continuous Data	20
	Post Hoc Pairwise Analyses	20
	Multivariable Statistics for Continuous Data: Linear Regression	21
	Conclusion	22
	References	23

4 Statistical Power and Power Calculations 25

Introduction 25

Selecting a Primary Outcome of Interest 26

Statistical Power and Power Calculations. 26

Post Hoc Power Calculations 29

Conclusion 29

References. 30

5 Characteristics of a Diagnostic Test: Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value 31

Introduction 31

Sensitivity 32

Specificity 32

Positive Predictive Value. 32

Negative Predictive Value 33

Accuracy Versus Precision 33

How Are Test Threshold Values Determined? ROC Curves. 34

Reference 36

6 Statistical Bias 37

Introduction 37

Selection Bias 38

Incorporation Bias. 39

Financial Bias 39

Information Bias 40

 Differential Misclassification 40

 Non-differential Misclassification. 41

 Other Types of Information Bias 41

Publication and Reporting Bias 42

References. 42

7 The Iterative Process of Designing Successful Clinical Research. 43

Introduction. 43

Formulating a Study Question 43

Operationalizing Variables 44

Directed Acyclic Graphs (DAGs) 45

Feasibility 46

Peer and Mentor Review. 46

The Iterative Process. 46

References. 47

Part II Choosing and Executing an Appropriate Clinical Study Design

8 Randomized Controlled Trials. 51

Study Mechanics. 51

Ideal Scenario for Prospective Randomized Controlled Trial Study Design 55

Statistical Analysis 55

Analytical Review	56
Reference	58
9 Case-Control Studies	59
Study Mechanics	59
Ideal Scenario for Case-Control Study Design	60
Statistical Analysis	61
Analytical Review	61
Reference	62
10 Cohort Studies	63
Study Mechanics	63
Ideal Scenario for Cohort Study Design	65
Cohort Study Patient Selection	65
Statistical Analysis	66
Analytical Reviews	67
References	69
11 Cross-Sectional Studies	71
Study Mechanics	71
Special Circumstances	72
Ideal Scenario for Cross-Sectional Study Design	73
Statistical Analysis	73
Analytical Review	74
Reference	75
12 Case Series and Case Reports	77
Study Mechanics	77
Ideal Scenario for Case Series and Case Reports	78
Statistical Analysis	78
Analytical Reviews	79
References	81
 Part III Specialized Study Designs	
13 Propensity Score-Matched Studies	85
Study Mechanics	85
Ideal Scenario for Propensity Score-Matched Studies	87
Statistical Analysis	87
Conclusion	87
Analytical Review	87
References	88
14 Interrater and Intrarater Reliability Studies	89
Study Mechanics	89
Statistical Analysis	91
Percent Agreement	91
Kappa	91

- Intraclass Correlation Coefficient 92
- Interpretation of Kappa and Intraclass Correlation Coefficient Values 94
- Analytical Review. 94
- References. 95
- 15 Clinical Outcome Scale Development and Validation 97**
- What Is a Clinical Outcome Scale? 97
- Patient-Reported Outcome Scale Development vs. Cross-Validation of an Existing Scale 97
- Scale Development and Pilot Testing 98
- Structure of Reliability and Validity Testing 99
- Reliability Testing. 100
- Construct Validity Testing. 100
- Translation and Cross-Cultural Adaptation. 101
- Analytical Review. 102
- References. 104
- Glossary 107**
- Index. 115**