

ESSENTIAL

# MEDICAL STATISTICS

Betty R. Kirkwood and Jonathan A. C. Sterne

SECOND EDITION



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# Essential Medical Statistics

## **Dedication**

To our children:  
Daisy and Sam Kirkwood  
Max, Kitty and Emily Sterne

SECOND EDITION

# Essential Medical Statistics

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## Preface to the second edition

The practice of medical statistics has changed considerably since the first edition was written. At that time the age of the personal computer was just beginning, and serious statistical analyses were conducted by specialist statisticians using main-frame computers. Now, there is ready access to statistical computing—even the most sophisticated statistical analyses can be done using a personal computer. This has been accompanied by the growth of the evidence-based medicine movement and a commitment of medical journals to improve the statistical rigour of papers they publish.

These changes mean that the boundary between what used to be considered ‘basic’ or ‘essential’ statistics and more advanced methods has been blurred. A statistical analysis presented in a leading general medical journal is more likely to use logistic regression (formerly considered a specialist technique) than to present results from  $\chi^2$  tests. In this second edition we describe the most commonly used regression models—multiple linear regression, logistic regression, Poisson regression and Cox regression—and explain how these include many basic methods as special cases. By including chapters on general issues in regression modelling, interpretation of analyses and likelihood, we aim to present a unified view of medical statistics and statistical inference, and to reflect the shift in emphasis in modern medical statistics from hypothesis testing to estimation. Other new chapters introduce methods, some relatively new, that allow common problems in statistical analysis to be addressed; these include meta-analysis, bootstrapping, robust standard errors, and analysis of clustered data.

Our aim throughout has been to retain the strengths of the first edition, by keeping the emphasis on enabling the reader to know which method to apply when. We have therefore structured the book into parts relating to the analysis of different types of outcome variable, and included new chapters on linking analysis to study design, measures of association and impact, and general strategies for analysis.

A number of the larger datasets used in the chapters on regression modelling are available for downloading from the book’s website ([www.blackwellpublishing.com/essentialmedstats](http://www.blackwellpublishing.com/essentialmedstats)), to allow readers to reproduce the analyses presented or try out further analyses for themselves. Readers are also invited to visit the website to check for corrections and updates and to give feedback, which we welcome.

In writing this second edition, we have benefited from advice and support from many colleagues, students and friends. In particular, we would like to thank the many readers who gave feedback on the first edition and inspired us to embark on this, Cesar Victora, Kate Tilling and Simon Cousens for so willingly commenting on early drafts in detail, David Clayton and Michael Hills for generous advice and unstinting help on many occasions, George Davey Smith for helpful comments on a number of draft chapters and the late Paul Arthur for his enduring encouragement and advice. We would like to express our appreciation to Christopher Baum, James Carpenter, Matthias Egger, Stephen Frankel, David Gunnell, Richard Hayes, Sharon Huttly, Mike Kenward, Peter McCarron, Roger Newson, Steven Oliver, Andrew Polmear, Bianca de Stavola, and Lesley Wood for helpful discussions and for sharing their insights into statistical issues. We are grateful to James Carpenter, Erik Christensen, Shah Ebrahim, Alison Elliot, Richard Hayes, David Kessler, Carl-Johan Lamm, Debbie Lawlor, Steven Oliver, Mary Penny, Seif Shaheen and Bianca de Stavola, who generously provided datasets for use as examples. We would also like to thank Maggie Rae and Alan Haworth, whose generous hospitality facilitated much writing, and last but not least Harriet Aston, Emily, Kitty and Max Sterne, Alex Khot, and Sam and Daisy Kirkwood, for their support and the difference they make in our lives.

Betty Kirkwood  
Jonathan Sterne

## Preface to the first edition

The aim in writing this book has been to put the multitude of statistical methods applicable to medical research into their practical context, and in doing this I hope I have combined simplicity with depth. I have adopted a somewhat different ordering of topics than found in most books, based on a logical progression of practical concepts, rather than a formal mathematical development. Statistical ideas are introduced as and when needed, and all methods are described in the context of relevant examples drawn from real situations. There is extensive cross-referencing to link and contrast the alternative approaches which may apply in similar situations. In this way the reader is led more quickly to the analysis of practical problems and should find it easier to learn which procedures are applicable and when.

This book is suitable for self-instruction, as a companion to lecture courses on medical statistics, and as a reference text. It covers all topics which a medical research worker or student is likely to encounter. Some advanced (or uncommon) methods are described only briefly, and the reader referred to more specialist books. It is hoped, however, that it will be a rare event to look for a topic in the index, and not to find even a mention. All formulae are clearly highlighted for easy reference, and there is a useful summary of methods on the inside front and back covers.

The book is a concise and straightforward introduction to the basic methods and ideas of medical statistics. It does not, however, stop here. It is intended also to be a reasonably comprehensive guide to the subject. For anyone seriously involved in statistical applications, it is not sufficient just to be able to carry out, for example, a  $t$  test. It is also important to appreciate the limitations of the simple methods, and to know when and how they should be extended. For this reason, chapters have been included on, for example, analysis of variance and multiple regression. When dealing with these more advanced methods the treatment concentrates on the principles involved and the interpretation of results, since with the wide availability of computing facilities it is no longer necessary to acquire familiarity with the details of the calculations. The more advanced sections may be omitted at a first reading, as indicated at the relevant points in the text. It is recommended, however, that the introductions of all chapters are read, as these put the different methods into context.

The reader will also find such topics as trend tests for contingency tables, methods of standardization, use of transformations, survival analysis and case-control studies. The last quarter of the book is devoted to issues involved in the design and conduct of investigations. These sections are not divorced in any way from the sections on methods of analysis and reflect the importance of an awareness of statistics throughout the execution of a study. There is a detailed summary of how to decide on an appropriate sample size, and an introduction to the use of computers, with much of the common jargon explained.

This book has been compiled from several years' experience both of teaching statistics to a variety of medical personnel and of collaborative research. I hope that the approach I have adopted will appeal to anyone working in or associated with the field of medical research, and will please medical workers and statisticians alike. In particular, I hope the result will answer the expressed need of many that the problem in carrying out statistical work is not so much learning the mechanics of a particular test, but rather knowing which method to apply when.

I would like to express my gratitude to the many colleagues, students, and friends who have assisted me in this task. In particular, I would like to thank David Ross and Cesar Victora for willingly reading early drafts and commenting in great detail, Richard Hayes for many discussions on teaching over the years, Laura Rodrigues for sharing her insight into epidemiological methodology with me, Peter Smith for comments and general support, Helen Edwards for patient and skilled help with the typing, and Jacqui Wright for assistance in compiling the appendix tables. I would also like to thank my husband Tom Kirkwood not only for comments on many drafts, endless discussions and practical help, but also for providing unfailing support and encouragement throughout. It is to him this book is dedicated. Finally, I would like to mention Daisy and Sam Kirkwood, whose birth, although delaying the finalization of an almost complete manuscript, provided me with an opportunity to take a fresh look at what I had written and make a number of major improvements.

Betty Kirkwood