Preventing and Treating Missing Data in Longitudinal Clinical Trials

A Practical Guide

Recent decades have brought advances in statistical theory for missing data, which, combined with advances in computing ability, have allowed implementation of a wide array of analyses. In fact, so many methods are available that it can be difficult to ascertain when to use which method. This book focuses on the prevention and treatment of missing data in longitudinal clinical trials. Based on his extensive experience with missing data, the author offers advice on choosing analysis methods and on ways to prevent missing data through appropriate trial design and conduct. He offers a practical guide to key principles and explains analytic methods for the non-statistician using limited statistical notation and jargon. The book's goal is to present a comprehensive strategy for preventing and treating missing data, and to make available the programs used to conduct the analyses of the example dataset.

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Preface

This book focuses on the prevention and treatment of missing data in longitudinal clinical trials with repeated measures, such as are common in later phases of medical research and drug development. Recent decades have brought advances in statistical theory, which, combined with advances in computing ability, have allowed implementation of a wide array of analyses. In fact, so many methods are available that it can be difficult to ascertain when to use which method. A danger in such circumstances is to blindly use newer methods without proper understanding of their strengths and limitations, or to disregard all newer methods in favor of familiar approaches.

Moreover, the complex discussions on how to analyze incomplete data have overshadowed discussions on ways to prevent missing data, which would of course be the preferred solution. Therefore, preventing missing data through appropriate trial design and conduct is given significant attention in this book. Nevertheless, despite all efforts at prevention, missing data will remain an ever-present problem and analytic approaches will continue to be an important consideration.

Recent research has fostered an emerging consensus regarding the analysis of incomplete longitudinal data. Key principles and analytic methods are explained in terms non-statisticians can understand. Although the use of equations, symbols, and Greek letters to describe the analyses is largely avoided, sufficient technical detail is provided so readers can take away more than a peripheral understanding of the methods and issues. For those with in-depth statistical interests, reference to more technical literature is provided.

Part I begins with illustrations of how missing data erode the reliability and credibility of medical research. Subsequent chapters discuss missing

data mechanisms and the estimands (what is to be estimated) of interest in longitudinal trials with incomplete data. Part II covers trial design and conduct features that can help prevent missing data. Part III includes chapters on common methods of estimation, data and modeling considerations, and means of dealing with missing data (e.g., imputation). Part IV ties together the topics covered in Part III to illustrate various analyses applicable to incomplete longitudinal data. Small example data sets are used to illustrate and explain key analyses. An actual clinical trial data set is the focal point for proposing and implementing an overall analytic strategy that includes sensitivity analyses for assessing the impact of missing data.

This strategy is referred to as the analytic road map. A road map is different from driving instructions. Unlike driving directions, a road map does not chart a specific course, with instructions on exactly how far to go and when to turn. Instead, the road map lays out the alternatives so that the best route for a particular situation can be chosen.

The concluding chapter refocuses on the key issues covered throughout the book, presents a comprehensive strategy for preventing and treating missing data, and makes available the programs used to conduct the analyses of the example dataset.