EPIDEMIOLOGY

Beyond the Basics

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To Hilda and Marion

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Preface

This book was conceived as an intermediate epidemiology textbook. Similarly to the first and second editions, the third edition explores and discusses key epidemiologic concepts and basic methods in more depth than that found in basic textbooks on epidemiology. For the third edition, new examples and exercises have been added to all chapters. In Chapters 7 and 10, respectively, we included discussions of novel epidemiologic strategies for handling confounding (i.e., instrumental variables and propensity scores) and of decision tree as a decision-making tool.

As an intermediate methods text, this book is expected to have a heterogeneous readership. Epidemiology students may wish to use it as a bridge between basic and more advanced epidemiologic methods. Other readers may desire to advance their knowledge beyond basic epidemiologic principles and methods but are not statistically minded and are thus reluctant to tackle the many excellent textbooks that strongly focus on epidemiology's quantitative aspects. The demonstration of several epidemiologic concepts and methods needs to rely on statistical formulations, and this text extensively supports these formulations with real-life examples, hopefully making their logic intuitively easier to follow. The practicing epidemiologist may find selected portions of this book useful for an understanding of concepts beyond the basics. Thus, the common denominators for the intended readers are familiarity with the basic strategies of analytic epidemiology and a desire to increase their level of understanding of several notions that are insufficiently covered (and naturally so) in many basic textbooks. The way in which this textbook is organized makes this readily apparent.

In Chapter 1, the basic observational epidemiologic research strategies are reviewed, including those based on studies of both groups and individuals. Although descriptive epidemiology is not the focus of this book, birth cohort analysis is discussed in some depth in this chapter because this approach is rarely covered in detail in basic textbooks. Another topic in the interface between descriptive and analytical epidemiology—namely, ecological studies—is also discussed, with a view toward extending its discussion beyond the possibility of inferential (ecological) bias. Next, the chapter reviews observational studies based on individuals as units of observation—that is, cohort and case-control studies. Different types of case-control design are reviewed. The strategy of *matching* as an approach by which to achieve comparability prior to data collection is also briefly discussed.

Chapters 2 and 3 cover issues of measurement of outcome frequency and measures of association. In Chapter 2, absolute measures of outcome frequency and their calculation methods are reviewed, including the person-time approach for the calculation of incidence density, and both the classic life table and the Kaplan-Meier method for the calculation of cumulative incidence. Chapter 3 deals with measures of association, including those based on relative (e.g., relative risk, odds ratio) and absolute (attributable risk) differences. The connections between measures of association obtained in

cohort and case-control studies are emphasized. In particular, a description is given of the different measures of association (i.e., odds ratio, relative risk, rate ratio) that can be obtained in case-control studies as a function of the control selection strategies that were introduced in Chapter 1.

Chapters 4 and 5 are devoted to threats to the validity of epidemiologic studies, namely bias and confounding. In Chapter 4, the most common types of bias are discussed, including selection bias and information bias. In the discussion of information bias, simple examples are given to improve the understanding of the phenomenon of misclassification resulting from less-than-perfect sensitivity and specificity of the approaches used for ascertaining exposure, outcome, and/or confounding variables. This chapter also provides a discussion of cross-sectional biases and biases associated with evaluation of screening procedures; for the latter, a simple approach to estimate lead time bias is given, which may be useful for those involved in evaluative studies of this sort. In Chapter 5, the concept of confounding is introduced, and approaches to evaluate confounding are reviewed. Special issues related to confounding are discussed, including the distinction between confounders and intermediate variables, residual confounding, and the role of statistical significance in the evaluation of confounding effects.

Interaction (effect modification) is discussed in Chapter 6. The chapter presents the concept of interaction, emphasizing its pragmatic application as well as the strategies used to evaluate the presence of additive and multiplicative interactions. Practical issues discussed in this chapter include whether to adjust when interaction is suspected and the importance of the additive model in public health.

The next three chapters are devoted to the approaches used to handle threats to the validity of epidemiologic results. In Chapter 7, strategies for the adjustment of confounding factors are presented, including the more parsimonious approaches (e.g., direct adjustment, Mantel-Haenszel) and the more complex (i.e., multiple regression, instrumental variables, Mendelian randomization, and propensity scores). Emphasis is placed on the selection of the method that is most appropriate for the study design used (e.g., Cox proportional hazards for the analysis of survival data or Poisson regression for the analysis of rates per person-time). Chapter 8 reviews the basic quality-control strategies for the prevention and control of measurement error and bias. Both qualitative and quantitative approaches used in quality control are discussed. The mostoften used analytic strategies for estimating validity and reliability of data obtained in epidemiologic studies are reviewed (e.g., unweighted and weighted kappa, correlation coefficients) in this chapter. In Chapter 9, the key issue of communication of results of epidemiologic studies is discussed. Examples of common mistakes made when reporting epidemiologic data are given as a way to stress the importance of clarity in such reports.

Chapter 10 discusses—from the epidemiologist's viewpoint—issues relevant to the interface between epidemiology, health policy, and public health, such as Rothman's causality model, proximal and distal causes, and Hill's guidelines. This chapter also includes brief discussions of three topics pertinent to causal inference: sensitivity analysis, meta-analysis, and publication bias; and consideration of the decision tree as a tool to evaluate interventions. As in the previous editions, Appendices A, B, C, and E describe selected statistical procedures (e.g., standard errors and confidence levels, trend test, test of heterogeneity of effects, intraclass correlation) to help the reader to more thoroughly evaluate the measures of risk and association discussed in the

text and to expose him or her to procedures that, although relatively simple, are not available in many statistical packages used by epidemiology students and practitioners. Appendix D includes two sections on quality assurance and control procedures taken from the corresponding manual of the Atherosclerosis Risk in Communities (ARIC) Study as examples of real-life applications of some of the procedures discussed in Chapter 8. Finally, Appendix F provides the answers to the exercises.

We encourage readers to advise us of any errors or unclear passages, and to suggest improvements. Please email any such suggestions or comments to: info@jblearning.com.

All significant contributions will be acknowledged in the next edition.

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To have enjoyed the privilege of teaching intermediate epidemiology for so many years made us realize how much we have learned from our students, to whom we are deeply grateful. Finally, without the support and extraordinary patience of all members of our families, particularly our wives, Hilda and Marion, we could not have devoted so much time and effort to writing the three editions of this text.

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