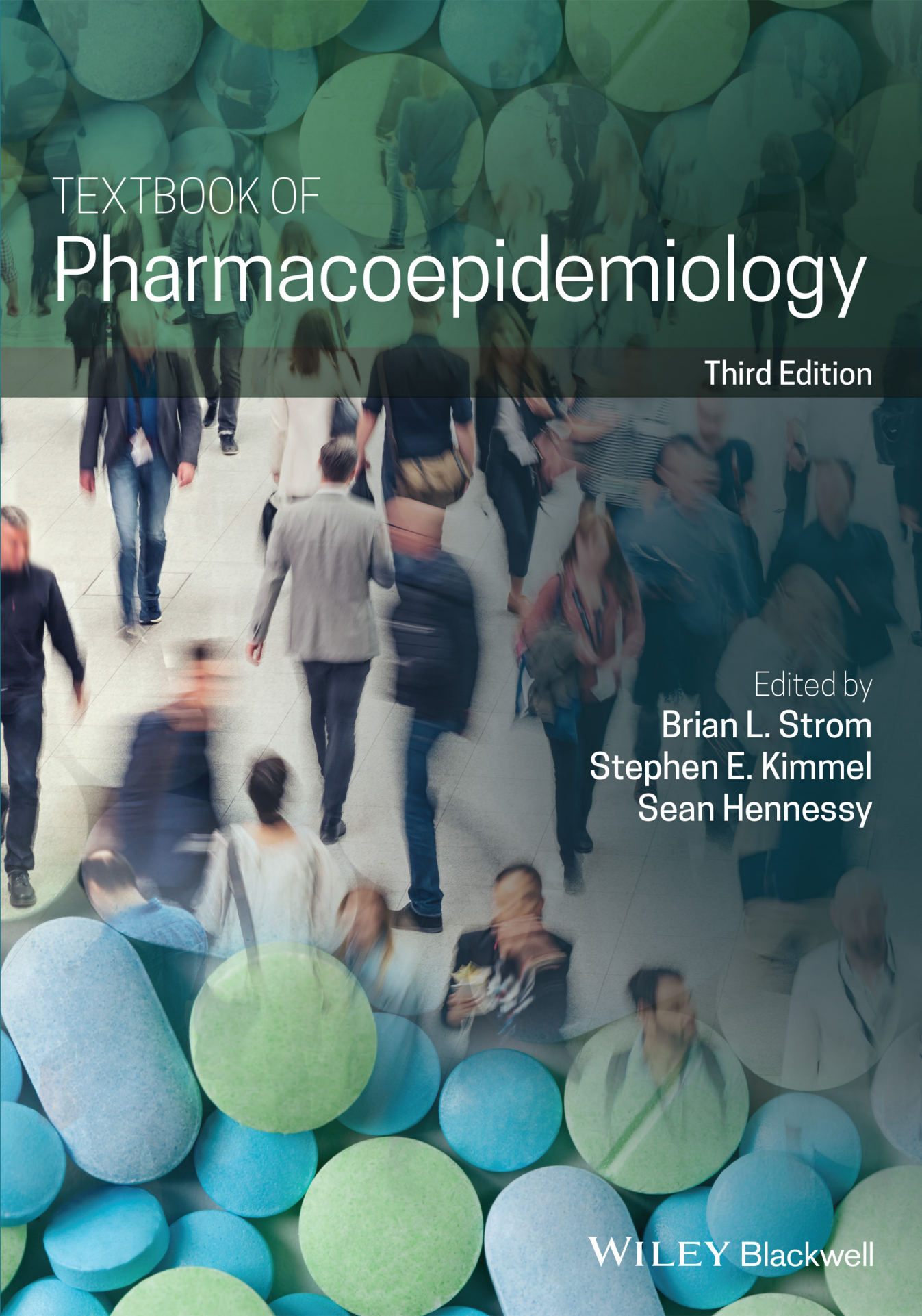
TEXTBOOK OF
Pharmacoepidemiology
Third Edition
Edited by
Brian L. Strom
Stephen E. Kimmel
Sean Hennessy
WILEY Blackwell

Textbook of Pharmacoepidemiology

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Third Edition

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Preface

It was a remarkable 33 years ago that the first edition of Strom's Pharmacoepidemiology was published. The preface to that book stated that pharmacoepidemiology was a new field with a new generation of pharmacoepidemiologists arising to join the field's few pioneers. Over the ensuing 32 years, the field indeed has grown and no longer deserves to be called "new." Many of those "new generation" scientists (including two of the editors of this book) are now "middle-aged" pharmacoepidemiologists. Despite its relatively brief academic life, a short history of pharmacoepidemiology and review of its current state will set the stage for the purpose of this textbook.

Pharmacoepidemiology originally arose from the union of the fields of clinical pharmacology and epidemiology. Pharmacoepidemiology studies the use of and the effects of medical products in large numbers of people and applies the methods of epidemiology to the content area of clinical pharmacology. This field represents the science underlying post-marketing medical product surveillance, studies of the effects of medical products (i.e. drugs, biologicals, devices) performed after a product has been approved for use. In recent years, pharmacoepidemiology has expanded to include many other types of studies, as well.

The field of pharmacoepidemiology has grown enormously since the first publication of Strom. The International Society of Pharmacoepidemiology, an early idea when the first edition of this book was written, has grown into a major international scientific force, with over 1476 members from 63 countries, an extremely successful annual meeting attracting more than 1800 attendees, a large number of very active committees and scientific interest groups, and its own journal. In addition, a number of established journals have targeted pharmacoepidemiology manuscripts as desirable. As new scientific developments occur within mainstream epidemiology, they are rapidly adopted, applied, and advanced within our field as well. We have also become institutionalized as a subfield within the field of clinical pharmacology, with scientific sections of the American Society for Clinical Pharmacology and Therapeutics and with pharmacoepidemiology a required part of the clinical pharmacology board examination.

Most of the major international pharmaceutical companies have founded dedicated units to organize and lead their efforts in pharmacoepidemiology, pharmacoeconomics, and quality-of-life studies. The continuing parade of drug safety crises emphasizes the need for the field, and some foresighted manufacturers have begun to perform "prophylactic" pharmacoepidemiology studies, to have data in hand and available when questions arise, rather than waiting to begin to collect data after a crisis has developed. Pharmacoepidemiologic data are now routinely used for regulatory decisions, and many governmental agencies have been developing and expanding their own pharmacoepidemiology programs. Risk evaluation and mitigation

strategies are now required by regulatory bodies with the marketing of new drugs, as a means of improving drugs' benefit/risk balance, and manufacturers are identifying ways to respond. Requirements that a drug be proven to be cost effective have been added to many national, local, and insurance health care systems, either to justify reimbursement or even to justify drug availability. A number of schools of medicine, pharmacy, and public health have established research programs in pharmacoepidemiology, and a few of them have also established pharmacoepidemiology training programs in response to a desperate need for more pharmacoepidemiology personnel. Pharmacoepidemiologic research funding is now more plentiful, and even limited support for training is available.

In the United States, drug utilization review programs are required, by law, of each of the 50 state Medicaid programs, and have been implemented as well in many managed care organizations. Now, years later, the utility of drug utilization review programs is being questioned. In addition, the Joint Commission requires that every hospital in the US have an adverse drug reaction monitoring program and a drug use evaluation program, turning every hospital into a mini-pharmacoepidemiology laboratory. Stimulated in part by the interests of the World Health Organization and the Rockefeller Foundation, there is even substantial interest in pharmacoepidemiology in the developing world. Yet, throughout the world, the increased concern by the public about privacy has made pharmacoepidemiologic research much more difficult to conduct.

In recent years, major new changes have been made in drug regulation and organization, largely in response to a series of accusations about myocardial infarction caused by analgesics, which was detected in long-term prevention trials rather than in normal use of the drugs. For example, FDA was given new regulatory authority after drug marketing. Further, the development, since 1 January 2006, of Medicare Part D, a US federal program to subsidize prescription drugs for Medicare recipients, introduced to pharmacoepidemiology a new database with a stable population approaching 50 million in what may be the largest healthcare system in the world. The US Congress has recognized the importance of the field, with the founding of the Sentinel Program, and new requirements that FDA focus on "real world evidence." A new movement has arisen in the US of "comparative effectiveness research," which in many ways learns from much longer experience in Europe, as well as decades of experience in pharmacoepidemiology. These developments portend major changes for our field.

In summary, there has been tremendous growth in the field of pharmacoepidemiology and a fair amount of maturation. With the growth and maturation of the field, Strom's *Pharmacoepidemiology* has grown and matured right along. *Pharmacoepidemiology* thus represents a comprehensive source of information about the field. As a reflection of the growth of the field, the fourth Edition of Strom was over twice as long as the first! Now, seven years after the fifth edition, the field continues to change and garner widespread interest, leading to the recent publication of the sixth edition in 2020.

So, why, one may ask, do we need a Textbook of Pharmacoepidemiology? The need arose precisely because of the growth of the field. With that, and the corresponding growth in the parent book, Strom's *Pharmacoepidemiology* has really become more of a reference book than a book usable as a textbook. Yet, there is increasing need for people to be trained in the field and an increasing number of training programs. With the maturity of the field comes therefore the necessity for both comprehensive approaches (such as Strom's *Pharmacoepidemiology*) and more focused approaches. Therefore, *Textbook of Pharmacoepidemiology* was intended as a modified and shortened version of its parent, designed to meet the need of students. We believe that students can benefit from an approach that focuses on the core of the discipline, along with learning aids.

Textbook of Pharmacoepidemiology attempts to fill this need, providing a focused educational resource for students. It is our hope that this book will serve as a useful textbook for students at all levels: upper-level undergraduates, graduate students, post-doctoral fellows, and others who are learning the field. To achieve our goals, we have substantially edited down from Strom's *Pharmacoepidemiology*, with a focus on what is needed by students, eliminating some chapters and shortening others. We also have provided case examples for most chapters and key points for all chapters. Each chapter is followed by a list of further reading.

So why update it? In looking at the sixth Edition of Strom, most chapters in the new edition were thoroughly revised to provide updated content. New chapters were added, along with many new authors. The second edition of the textbook was simply getting out of date in comparison to the recently published sixth edition of the parent book.

Specifically, we have tried to emphasize the methods of pharmacoepidemiology and the strengths and limitations of the field, while minimizing some of the technical specifications that are important for a reference book but not for students. Therefore, the first five chapters of Part I, "Introduction to Pharmacoepidemiology," lay out the cores of the discipline, and remain essentially unchanged from Strom's *Pharmacoepidemiology*, with the exception of the inclusion of key points and lists of further reading. We have also included a chapter on different perspectives of the field (from academia, industry, regulatory agencies, and the legal system), as a shortened form of several chapters from the reference book. Part II focuses on "Sources of Pharmacoepidemiology Data" and includes important chapters about spontaneous pharmacovigilance reporting systems, electronic databases, and other approaches to pharmacoepidemiology studies. Part III summarizes "Special Issues in Pharmacoepidemiology Methodology" that we feel are important to more advanced pharmacoepidemiology students. Although no student is likely to become an expert in all of these methods, they form a core set of knowledge that we believe all pharmacoepidemiologists should have. In addition, one never knows what one will do later in one's own career, nor when one may be called upon to help others with the use of these methods. Part IV concludes the textbook with a collection of "Special Applications" of the field, and speculation about its future, always an important consideration for new investigators in charting a career path.

Pharmacoepidemiology may be maturing, but many exciting opportunities and challenges lie ahead as the field continues to grow and respond to unforeseeable future events. It is our hope that this book can continue to serve as a useful introduction and resource for students of pharmacoepidemiology, both those enrolled in formal classes and those learning in "the real world," who will respond to the challenges that they encounter. Of course, we are always students of our own discipline, and the process of developing this textbook has been educational for us. We hope that this book will also be stimulating and educational for you.

Brian L. Strom, MD, MPH.
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John Hemphill's contributions to this book were instrumental, encompassing the role of project manager where he coordinated the entire process of contacting the authors and pulling the book together, while additionally providing editorial assistance.

BLS would like to thank Steve Kimmel and Sean Hennessy for joining him as co-editors. Steve did the bulk of the work on the first edition of this textbook, and Steve and Sean joined BLS as co-editors for the fifth and sixth edition of the parent book, *Pharmacoepidemiology*. These are two very special and talented men. It has been BLS's pleasure to help train them – now, too many years ago – help them cultivate their own careers, and see them blossom into star senior pharmacoepidemiologists. It is wonderful to be able to share with them this book, which has been an important part of BLS's life and career.

BLS would also like to thank his parents, now deceased, for the support and education that were critical to him being successful in his career. BLS would also like to thank the late Paul D. Stolley, M.D., M.P.H. and the late Kenneth L. Melmon, M.D., for their direction, guidance, and inspiration in the formative years of his career. He would also like to thank his trainees, from whom he learns at least as much as he teaches. Last, but certainly not least, BLS would like to thank his family – Lani, Shayna, and Jordi – for accepting the time demands of the book, for tolerating his endless hours working at home (on its earlier editions, for the kids), and for their ever present love and support.

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Part I

Introduction to Pharmacoepidemiology