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Evidence-Based Diagnosis

An Introduction to Clinical Epidemiology

Second Edition

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TOM: I would like to thank my wife, Johannah, and children, David and Rosie, for their support on the long road that led to the publication of this book. I dedicated the first edition to my parents, Ed and Carol Newman, in whose honor I donated my share of the royalties to Physicians for Social Responsibility (PSR), in support of its efforts to rid the world of nuclear weapons. There was good news on that front! In 2017, ICAN, the International Coalition to Abolish Nuclear Weapons (started by International Physicians for the Prevention of Nuclear War, of which PSR is the US affiliate), won the Nobel Peace Prize for its successful work on a United Nations Nuclear Weapons Ban Treaty! But much work remains to be done, so I reaffirm my commitment to donate all of my royalties to PSR, in memory of my late parents.

MICHAEL: I again thank my wife, Caroline, and children, Emily, Jake, and Kenneth, and dedicate this book to my mother, Jean Kohn, MD, MPH, and my late father, Martin Kohn, MD.

MARTINA: I would like to thank Tom Newman and Michael Kohn for letting me be part of this journey, and my husband Marc for his support and patience when I was buried behind the computer, designing the figures. I dedicate this book to my parents, Suzanne and Thomas Mueller.

This book is a labor of love. Let us know how you like it!

In solidarity,

Tom, Michael, and Martina

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Preface

This is a book about diagnostic testing. It is aimed primarily at clinicians, particularly those who are academically minded, but it should be helpful and accessible to anyone involved with selection, development, or marketing of diagnostic, screening, or prognostic tests. Although we admit to a love of mathematics, we have restrained ourselves and kept the math to a minimum – a little simple algebra and only three Greek letters, κ (kappa), α (alpha), and β (beta). Nonetheless, quantitative discussions in this book go deeper and are more rigorous than those typically found in introductory clinical epidemiology or evidence-based medicine texts.

Our perspective is that of skeptical consumers of tests. We want to make proper diagnoses and not miss treatable diseases. Yet, we are aware that vast resources are spent on tests that too frequently provide wrong answers or right answers of little value, and that new tests are being developed, marketed, and sold all the time, sometimes with little or no demonstrable or projected benefit to patients. This book is intended to provide readers with the tools they need to evaluate these tests, to decide if and when they are worth doing, and to interpret the results.

The pedagogical approach comes from years of teaching this material to physicians, mostly fellows and junior faculty in a clinical research training program. We have found that many doctors, including the two of us, can be impatient when it comes to classroom learning. We like to be shown that the material is important and that it will help us take better care of our patients, understand the literature, and/or improve our research. For this reason, in this book we emphasize real-life examples.

Although this is primarily a book about diagnosis, two of the twelve chapters are about evaluating treatments – using both randomized trials (Chapter 8) and observational studies (Chapter 9). The reason is that evidence-based diagnosis requires being able to quantify not only the information that tests provide but also the *value* of that information – how it should affect treatment decisions and how those decisions will affect patients' health. For this last task we need to be able to quantify the effects of treatments on outcomes. Other reasons for including the material about treatments, which also apply to the material about P-values and confidence intervals in Chapter 11, are that we love to teach it, have lots of good examples, and are able to focus on material neglected (or even wrong) in other books.

The biggest change in this second edition is the addition of color and new illustrations by Dr. Martina Steurer, a graphic artist who also is a neonatologist and pediatric intensivist. Martina, a 2012 alumna of the clinical epidemiology course for which this book is the prescribed text, joined the teaching team of this course in 2015. We hope you will find this edition as visually pleasing as it is intellectually satisfying.

As with the first edition, we include answers to all problems at the back of the book. We will continue to share new ones on the book's website (www.EBD-2.net). The website also features a virtual slide rule to help readers visualize the calculation of the posterior probability of disease and an online tool that produces regret graphs like those in Chapters 2 and 3 to aid in visualizing the tradeoff between false-positives, false-negatives, and the cost of a test. Take a look!

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This book started out as the syllabus for a course Tom first taught to Robert Wood Johnson Clinical Scholars and UCSF Laboratory Medicine Residents beginning in 1991, based on the now-classic textbook *Clinical Epidemiology: A Basic Science for Clinical Medicine* by Sackett, Haynes, Guyatt, and Tugwell [1]. Although over the years our selection of and approach to the material has diverged from theirs, we enthusiastically acknowledge their pioneering work in this area.

We thank our colleagues in the Department of Epidemiology and Biostatistics, particularly Dr. Stephen Hulley for his mentoring and Dr. Jeffrey Martin for his steadfast support. We also thank our students, who have helped us develop ways of teaching this material that work best and who have enthusiastically provided examples from their own clinical areas that illustrate the material we teach. Many of the problems we have added to the book began as problems submitted by students as part of our annual final examination problem-writing contest. (Their names appear with the problem titles.) We particularly thank the students who took Epi 204 in 2017 and 2018 and made suggestions on chapter drafts or problems for this second edition.

Reference

1. Sackett D, Haynes RB, Guyatt GH, Tugwell P. *Clinical epidemiology: a basic science for clinical medicine*. Boston: Little, Brown and Company; 1991.

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