Book Review

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Human Genome Epidemiology. Edited by Muin J. Khoury, Julian Little, and Wylie Burke. New York: Oxford University Press, 2004. Pp. 549.

The development of new molecular tools and computational methods for the study of human genetic diseases and traits has led to a wave of excitement about the implications of genetic discoveries. These advancements apply not only to rare genetic disorders but also to common complex genetic traits, and they have the potential to improve health and prevent disease. The implementation of such discoveries inevitably requires multidisciplinary expertise, which is clearly represented in *Human Genome Epidemiology,* edited by Muin Khoury, Julian Little, and Wylie Burke. The diverse academic backgrounds of the contributors reflect the multidisciplinary nature of this field. Although the focus of this book is on public health genetics, several aspects of human genetics research are covered, including some statistical genetics concepts as well as ethical, legal, and social issues.

This book is in the same vein as a previously published book entitled *Genetics and Public Health in the 21st Century* and is a complement to the book *Fundamentals of Genetic Epidemiology,* which also has Muin Khoury as its leading editor. In the present book, Khoury, Little, and Burke define the term "Human Genome Epidemiology" (HuGE) as "the application of the epidemiologic approach to the human genome in relation to health and disease." Although the book covers a wide continuum from gene discovery to the development and application of genetic tests, the focus of this book is on the approach to take after genes for complex traits have been identified. This book has been organized into four sections, which are presented and briefly commented on below.

Part I of the book, "Fundamentals," opens with "Human Genome Epidemiology: Scope and Strategies" (chapter 1), providing an introduction to the field of HuGE research. Chapter 2 briefly presents the fundamentals of technologies and the methods for gene discovery, including descriptions of various types of genetic markers, genotyping methods, and proteomic technologies. In chapter 3, the most common approaches for determining the genetic basis of diseases and for identifying the genes underlying complex traits are briefly presented. Ethical, legal, and social issues related to HuGE studies, including topics such as informed consent, are presented in chapter 4.

In Part II, "Methods and Approaches I: Assessing Disease Associations and Interactions," epidemiologic design strategies and analytic methods used in genetic association studies are presented. This includes the assessment of gene-gene interaction and gene-environment interaction, as well as challenges inherent in such studies. Factors to consider in specimen selection for genetic epidemiologic studies, as well as some quality-assurance measures, are discussed in chapter 5. A very clear and concise review of statistical issues in the design and analysis of gene-disease association studies is presented in chapter 6. Chapters 7–9 present various fundamental units of epidemiologic analyses of studies that relate health outcomes and issues relevant to gene-environment studies. This section ends with recommendations for reporting and reviewing HuGE studies (chapter 10).

Part III, "Methods and Approaches II: Assessing Genetic Tests for Disease Prevention," addresses the application of genetic epidemiologic methods to both clinical and public health settings. Various issues surrounding the evaluation and implementation of genetic testing in populations are covered, including analytic and clinical validity and the clinical utility of genetic tests (chapter 11). In particular, chapter 12 presents an evidence-based approach to genetic testing in populations, and chapter 13 presents a model process for evaluating data on newly developed genetic tests, aiming to provide summary data that could be useful, for example, to policy makers and public health administrators. Chapter 14 is on pharmacogenomics, and chapter 15 covers the integration of genetics into randomized controlled trials. Chapters 16 and 17 present a U.S. perspective on the clinical use of genetic tests and a U.K. perspective on the development of genetics services, respectively.

Part IV, "Case Studies: Using Human Genome Epidemiology Information to Improve Health" (chapters 18–29), provides an illustration of concepts discussed earlier in the book, including examples of single-gene disorders as well as complex diseases. Each example presented in this section highlights the necessity of obtaining population-level information required for health policy development and novel approaches to clinical practice.

The strengths of this book lie in its comprehensive treatment of this timely subject and in the richness of applied examples and clear tables. Overall, the book provides a broad covering of aspects related to public health genetics. It presents the current knowledge, identifies gaps in HuGE studies, and provides recommendations on the challenging work that remains to be done. The practical information included in this book is quite useful in providing direction in several areas. For example, a clear table in chapter 5 compares the various types of DNA specimens that can be used for epidemiologic studies, the quantity of DNA that can be collected from each kind of sample, and the advantages and disadvantages of each type of specimen. Chapter 10 presents a checklist for reporting and appraising studies of gene association and characterization studies. Chapter 16 discusses the evidence needed for practice

guidelines related to genetic testing, as well as strategies available to clinicians and policy makers to accomplish this task.

A relative weakness of the book, which may be inherent in such a complex, multidisciplinary, multi-authored effort, is that some sections are redundant. For example, population stratification is presented and discussed in eight chapters, and clinical validity and utility is covered in several chapters as well. Moreover, some chapters, such as chapters 7 and 10, are partially copied from published review articles. Finally, given that this book is multidisciplinary and is likely to have readers that may be unfamiliar with some of the genetics terminology, a glossary of the terms used in this book would have been beneficial.

This book, *Human Genome Epidemiology,* can be used as a reference tool or a self-teaching resource. It will be useful to epidemiologists and public health researchers who are interested in the applications of genetics research, as well as teachers in these fields who are looking for examples to help students understand concepts related to public health genetics. This book highlights the considerations that should be made prior to translating gene discoveries into a public health context. It could also be useful to clinicians and policy makers who want an overview of the present stage of research in this area. I would not, however, recommend this volume as a textbook, because, despite being comprehensive, it does not provide sufficient detail in individual areas to ensure in-depth understanding by students. This book finds its niche by presenting genetics from a broad public health perspective, an area in which books are currently relatively scarce.

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