Book Review

Network Meta-Analysis: Evidence Synthesis With Mixed Treatment Comparison
Edited by Giuseppe Biondi-Zoccai

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Systematic reviews and meta-analyses, being at the intersection of clinical medicine, epidemiology, statistics, and translational research, are key methodologies for the practice of evidence-based medicine (1, 2). Traditional meta-analytical methods, however, pertain to pairwise comparisons between 2 interventions, thus only partially providing evidence that patients, clinicians, and policy-makers need in order to make informed decisions or public health recommendations regarding prevention, screening, diagnosis, and treatment. Questions similar to the following are often encountered in clinical practice. When there are direct (i.e., head-to-head) comparisons for only a few of the numerous biological agents for the treatment of rheumatoid arthritis, which one will have the greatest benefit in relieving joint pain? Which of the dozens of antidepressants are more likely to be effective in comparison with all other drugs in improving the symptoms of depression; are all of them equal, or is there a ranking as far as their effectiveness and safety profiles are concerned?

Recent statistical advances have resulted in the development of methodologies that allow the estimation of efficacy metrics (such as relative risks or risk differences) for all possible comparisons in a body of evidence, regardless of whether there have been direct head-to-head comparisons in clinical trials. These methods are collectively known as network meta-analysis (NMA) or multiple-treatments meta-analysis (3), and they constitute some of the latest tools in the array of evidence-based medicine for evaluating networks of interventions. Although there are many excellent introductory and advanced textbooks (4–7) covering all aspects of systematic reviews and pairwise meta-analysis, there was no such textbook for NMA until the publication of *Network Meta-Analysis: Evidence Synthesis With Mixed Treatment Comparison*, edited by Dr. Giuseppe Biondi-Zoccai.

As of October 2014, there were already more than 460 indexed citations in PubMed with the terms "network meta-analysis" or "multiple-treatments meta-analysis" in their title or abstract. This number is expected to increase quickly as clinicians and researchers become more familiar with this study design and as the merits of these analyses become more widely recognized by practitioners of evidence-based medicine. This makes the book very timely, especially since there is no other textbook that covers the recent advances in this novel area. Both researchers and consumers of evidence-based medicine (mainly clinicians and policy-makers) would benefit from a reference textbook on NMA, which gradually gains the lion's share in the hierarchy of evidence. The book greatly serves this purpose by summarizing the current status of the field in 22 chapters organized into 7 sections. The book is structured so that both beginners and people with more advanced knowledge of the topic can follow it as well as refer to it abstractly, focusing on specific issues that are of most interest. Hence, it provides a detailed and comprehensive overview of the statistical and methodological advances in NMA that have been sporadically published as original research or review articles in clinical and statistical journals, while at the same time it extends many of these methods.

Who will find the book useful? Students and researchers in biostatistics and clinical epidemiology will find it a useful introduction not only to NMA but also to concepts that are common to traditional (pairwise) meta-analysis and NMA. For researchers involved in the conduct of NMA, the book will serve as a quick reference guide to the latest methods and available software for obtaining summary estimates and evaluating biases in NMAs, which are described in great statistical detail. Finally, for clinicians who regularly review the literature in order to provide evidence-based care to their patients, the book can supply detailed guidance on how to read and interpret the results of published NMAs—which is particularly challenging, since these studies may involve more complex statistical methods than traditional meta-analysis. Overall, the book offers a valuable summary of the current practices in NMA for a diverse audience.

Despite a partial overlap in the concepts discussed among some chapters (unavoidable given the large number of contributing authors), the book delineates all of the steps that are required for the successful design, analysis, interpretation, and reporting of an NMA. After a necessary connection between pairwise and network meta-analysis is made in chapters 1 and 2, the reader is introduced to the prerequisites of a successful meta-analysis, including the recently adopted guidance on protocol registration and issues related to the systematic review and appraisal of evidence (chapters 3–6). After reviewing the literature and identifying the eligible studies, a meta-analyst faces the challenging task of selecting appropriate statistical models for analysis of the extracted data (chapters 7–9). Both the analysis and the interpretation require researchers to carefully address the issues of heterogeneity, inconsistency, and bias, as well as to present the results of their NMA in a concise and informative way (chapters 10–15). Finally, the case studies from various medical specialties (chapters 16–20) provide real-world examples of the concepts discussed in the previous chapters. The book closes with some looks into the future of the field (chapters 21 and 22), which is currently being transformed by methodological advances and numerous applications of NMA.

What is missing from the book? Reading the sections on the different statistical packages and software that are currently available, I felt that a website with real or simulated data sets would be a useful companion for readers wishing to exercise their technical skills. In general, although the issue of software is covered at some points throughout the book, this is not done in a systematic way that would allow the reader to learn the specific technical details. An appendix with guidance on implementation would probably be worth adding, especially since this is a very new field.

As Dr. Biondi-Zoccai notices in the preface, "[it is hoped] that this book will become obsolete and useless in 5 years or less" (p. xxxv). Although a paradox, this is particularly true, as the field is rapidly evolving with the development of new methods and the application of NMA not only to summary-level data but also to individual-patient data. Therefore, it is very likely that new books will appear soon covering the newest approaches that unavoidably will become available after the publication of this book. Nonetheless, *Network Meta-Analysis: Evidence Synthesis With Mixed Treatment Comparison* serves as a useful start for investigators who plan to conduct an NMA, as well as for those who are most interested in understanding published results from NMAs so they can apply the findings to their evidence-based clinical practice.

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