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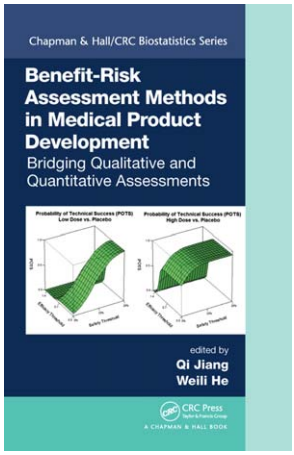
BOOK REVIEW

Benefit-Risk Assessment Methods in Medical Product Development: Bridging Qualitative and Quantitative Assessments



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Benefit-risk assessments, which evaluates the benefits of a medical product, device, or intervention, as well as its associated risks, is increasingly utilized to assist in decision making at regulatory agencies, within pharmaceutical companies, and by clinical practitioners. At its core, benefit-risk is about trade-offs – trying to understand the type, magnitude, and likelihood of benefits a patient may receive offset by the type, severity, magnitude, and likelihood of the risks a patient may incur from an intervention. However, a means of standardizing such assessments has not been established. In addition, it may be difficult to account for uncertainty with the available data or to formally account for the patient perspective in the decision making. As such, under many circumstances, informal, subjective assessments are conducted to inform decision making, often based on prior experience. This text, which was written by several excellent scientists and statisticians from industry, regulatory agencies, and academia, seeks to address this gap and provides a systematic review of benefit-risk assessments. In addition, the text outlines some applications, approaches, statistical considerations, and examples of benefit-risk assessments in the context of available data.

Section I provides an introduction on the role of benefit-risk assessment in drug development, regulation, and clinical practice, highlighting the importance of a common, transparent benefit-risk framework to inform decision making.

Section II provides an overview on worldwide regulatory policy initiatives with regards to benefit-risk assessment, with a particular focus on efforts from the US Food and Drug Administration (FDA) and European Medicines Agency. More detail is given to guidance development and the decision-making process at the US FDA Center for Devices and Radiological Health (CDRH), including the importance of patient voice during benefit-risk determination.

Section III tackles how to conduct a quantitative benefit-risk assessment; one might go about understanding uncertainties in the data, selecting events of interests, and weighing multiple events in an assessment. Various subgroups may also display varying levels of treatment benefit or risk. When grounded in understanding of the disease and the drug's mechanism of action, these subgroup analyses could inform how to optimize a treatment. Although one may think of benefit-risk in the context of a population, this section highlights that benefit-risk assessments can be a patient-level consideration. Even an individual's judgments and preferences could be counted as part of benefit-risk assessment. The section also highlights the various data sources that may be used, including clinical trial data, data from observational studies, spontaneous reporting of event postmarketing, and registries. The uncertainty associated with premarketing and postmarketing data sources is a key consideration when determining the feasibility and interpreting the results of a benefit-risk analysis.

Section IV provides details regarding statistical or nonstatistical methods and visualization tools to facilitate benefit-risk assessments. It highlights the importance of a transparent representation of weighting, event selection, and methods as these all can impact final assessments. Some cases may involve a single pair of events, whereas other cases may require a weighted combination of multiple beneficial and harmful outcomes. Due to the complexities of benefit-risk analyses, one should consider multiple techniques for visualizing the results.

The final section (Section V) gives multiple case studies, including various drug (vorapaxar, prasugrel, dabigatran, rivaroxaban, and natalizumab) and device examples (optimal retrieval times for inferior vena cava filters). This is a fantastic list in which the lessons from the book are applied and illustrate how conclusions may have been reached by regulatory agencies.

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One limitation of the book is that only the major results for the benefit-risk assessment are provided. References to the analyses are provided, but example codes for conducting such an analysis are not included. Another point worth mentioning is that the benefit-risk weights and selection of events rely on expertise across many different disciplines. Therefore, a vast collaboration across clinicians, statisticians, outcome researchers, commercial personnel, regulatory agencies, and patients are needed to standardize and improve benefit-risk assessments. Overall, this book provides a good summary of what goes into a benefit-risk assessment, what are crucial components for conducting such an analysis, and where such analyses have been used to inform treatment decisions. I would recommend this book as an excellent starting point for someone interested in learning more about the rationale and considerations for conducting a benefit-risk assessment.