

# Methodological Guidelines and Publications of Benefit-risk Assessment for Health Technology Assessment: A Scoping Review

EIXO 2: IMPLEMENTAÇÃO DE TECNOLOGIAS E DIRETRIZES CLÍNICAS EM SAÚDE

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**Introduction:** Benefit-risk assessment (BRA) is an important component in decision-making throughout the lifecycle of a health technology. The BRA of comparative technologies was usually carried out informally, without the use of a systematized process, which can lead to inappropriate decisions. In the last two decades, efforts have been observed to use more structured, objective and transparent approaches, aiming at better communication and decision-making by stakeholders. In this sense, some frameworks have been proposed to guide BRA, and are currently available. Therefore, we conducted a scoping review to: (1) map the available methodological guidelines and documents for conducting and reporting BRA in the different phases of the lifecycle of health technologies; and (2) identify methodological guidelines on methods for BRA, which could be used as the basis for the development of a BRA guideline for the Brazilian Health Technology Assessment (HTA) context.

**Methods:** Our searches were conducted between Oct 2022 to Mar 2023 in three main sources: (1) electronic databases (EMBASE and MEDLINE); (2) grey literature (48 HTA and regulatory organizations); and (3) manual search and contacting experts in the field. We included methodological guidelines or publications presenting methods for conducting or reporting BRA of any types of health technologies developed in any context of the health technology's lifecycle. Selection process and data charting were conducted by pairs of independent reviewers. We provided a narrative synthesis of the findings.

**Results:** From the 83 eligible documents, only six stated the HTA context, 30 were produced in the regulatory setting and 35 documents involved guidance for BRA throughout the health technology's lifecycle. Among the 129 methodological approaches for BRA identified, the most frequently cited descriptive frameworks were the Problem, Objectives, Alternatives, Consequences, Trade-offs, Uncertainty, Risk, and Linked decisions (ProACT-URL) and the Benefit Risk Action Team (BRAT), reported in 29 (34.9%) of the documents. Multicriteria Decision Analysis was the most common quantitative framework, cited in 52 (62.7%) of the documents. Other frequent quantitative frameworks cited were Markov Decision Process (n=18; 21.7%) and Decision Tree (n=16; 19.3%). We also identified the most cited metric indices which could be used to measure benefits and risks: numbers needed to harm (n=38; 45.8%) and to treat (n=37; 44.6%) as threshold indices, quality-adjusted life-year (n=37; 44.6%) as health index, and incremental net health benefit (n=32; 38.6%) as trade-off index. The documents also report probabilistic simulation method (n=32; 38.6%) and indirect treatment comparison (n=18; 21.7%) as the most common estimation techniques, while discrete choice experiment and conjoint analysis, mentioned in 26 (31.3%) documents, were the most mentioned utility survey techniques to elicit preferences for quantitative BRA.

**Discussions and conclusions:** The efforts for using formal structure approaches for BRA in HTA and at population level have been more modest than in the regulatory setting. We will test and explore the potential of the two most cited descriptive and quantitative frameworks in case studies in the context of HTA to evaluate their performance. The case studies using the frameworks identified in this review will support the elaboration of the Brazilian guideline of BRA for HTA.

**Keywords:** Health Technology Assessment; Benefit-Risk Assessment; Benefit-Risk Evaluation; Methodological Guidelines; Methodological Guidance; Scoping Review