Guidance for the Economic Evaluation of Prognostic and Predictive Companion Diagnostics: A Systematic Scoping Review

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BACKGROUND

Companion diagnostics (CDx) play a critical role in precision medicine, providing crucial information to guide the safe and effective use of therapeutic interventions by identifying patients most likely to benefit from targeted therapies[1]. However, economic evaluations of CDx are challenging due to their indirect impact on outcomes[2]. Prognostic and predictive CDx add complexity by providing continuous measures related to disease progression and treatment response[3]. Despite existing guidance, there are no studies focusing on economic evaluations of CDx with prognostic and predictive capabilities[1-2,4-6].

OBJECTIVES

This study aims to provide guidance on integrating prognostic and predictive CDx (pCDx) into health economic models, building upon literature that emphasizes the importance of clinical validity and utility.

METHODS

This scoping review followed a registered protocol[7] and PRISMA-ScR guidelines. Searches were performed in MEDLINE and Scopus from January 2008 to March 2023. The search strategy combined terms for "economic evaluation," "companion diagnostics," and "modeling methods." Independent reviewers performed study screening, selection, and data extraction. The included economic evaluations were examined for key methodological considerations relevant to pCDx economic evaluation.

RESULTS

The search yielded 2,591 potentially relevant studies. After duplication removal, 2,352 studies were screened, and 162 were selected for full-text review. Of these, 102 studies were excluded due to irrelevance, leaving 60 studies for inclusion. Detailed information on the selection process is provided in the PRISMA diagram (Figure 1). The six considerations to guide the economic evaluations of pCDx are described in Table 1.

SUMMARY OF THE INCLUDED ECONOMIC EVALUATIONS:

- Most studies were conducted in Europe (43%) and the USA (35%).
- The most common therapeutic area was breast cancer (55%).
- Most pCDx targeted chemotherapy decision-making (60%).
- Markov models (37%) and decision tree-Markov hybrids (30%) were the most used modeling methods.
- Quality-adjusted life years were the primary outcome in 88% of studies, with the healthcare perspective used in 70%.
- Deterministic sensitivity analysis was the most common robustness testing method (83%).
- Only 8% of studies evaluated pCDx with AI capabilities

1.	**Incorporating sensitivity and specificity:** Use Bayesian methods to accurately reflect conditional probabilities and real-world effectiveness of the pCDx.
2.	**Distinguishing clinical validity from clinical utility:** Incorporate decision impact data to reflect actual clinical practice, considering compliance and patient/clinician preferences.
3.	**Considering the pre-test probability:** Ensure pre-test probability (prevalence) is incorporated in the model and it accurately represents the whole target population.
4.	**Including the impact of false predictions:** Account for false positives and negatives to avoid skewed results.
5.	**Specifying the cut-off threshold for action:** Vary cut-off thresholds to assess their impact on cost-effectiveness, and ideally, identify the optimal threshold from cost-effectiveness perspective.
6.	**Accounting for multifactorial decision making:** Model the combined clinical utility of multiple pCDx tests rather than their individual accuracies.

Table 1. Six considerations based on review to guide the economic evaluation of pCDx

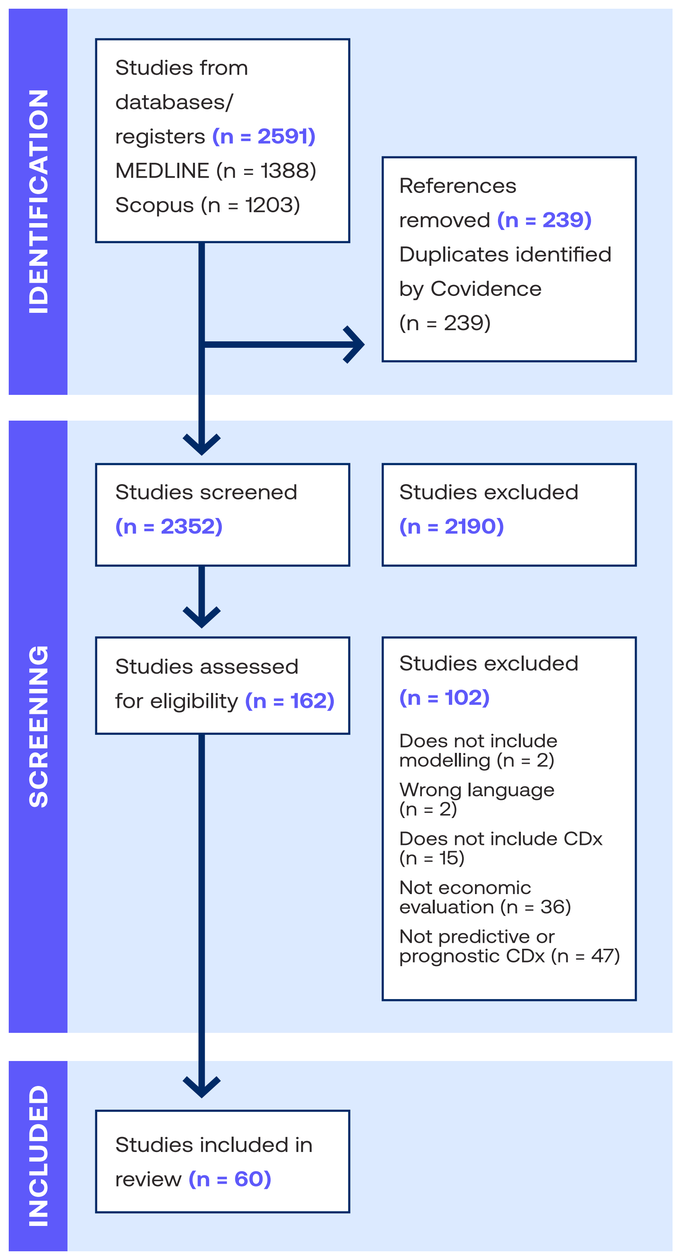

Figure 1. PRISMA diagram

CONCLUSIONS

This review highlights several challenges in evaluating the economic impact of pCDx, especially in integrating clinical utility and test accuracy. Variations in patient adherence and physician preferences further complicate downstream effects. We propose six considerations to improve pCDx evaluations. Future research should focus on model transparency, real-world data integration, and refining methods, particularly for AI-driven diagnostics, to enhance their incorporation into HTA and reimbursement processes.

References

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