A systematic scoping review to identify challenges in the economic evaluation of prognostic and predictive companion diagnostics in personalized medicine: The RadioVal study

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BACKGROUND

Companion diagnostics (CDx), which are tools used to tailor medical treatments to individual patients, play a pivotal role in the realization of personalized medicine (PM)[1]

CDx can aid in diagnosis (diagnostic), assess outcomes (prognostic) or predict intervention response (predictive)[2]

Evaluating CDx is known to be inherently complex, partly due to the intricate nature of assessing their indirect influence on patient outcomes[2]

Numerous reviews have delved into the economic evaluation of CDx within the framework of PM[3-6].

However, the existing body of literature has mainly focused on economic evaluations of diagnostic tests, leaving a notable gap in our comprehension of the economic assessment of prognostic and predictive companion diagnostics (pCDx).

OBJECTIVE

The aim of this systematic scoping review is to **examine the challenges associated with the economic evaluation of prognostic and predictive companion diagnostics** in the context of personalized medicine.

METHODS

The scoping review adhered to our published protocol

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and the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping review (PRISMA-ScR) statement.

We performed searches in MEDLINE and Scopus, from January 2008 to March 2023

Inclusion criteria were defined by relevant key words and medical subject headings were categorized into three branch topics separated by an “AND” operator:

1. Economic evaluation
   AND
2. Companion diagnostics
   AND
3. Modelling methods

Screening and data extraction were conducted by two independent reviewers. Conflicts were resolved with the aid of a third reviewer.

A descriptive analysis of the extracted data was conducted to identify challenges most frequently found in the included studies.

RESULTS

Out of 2,589 studies initially identified, **96 (3.7%) met our inclusion criteria** based on their relevance to the research objectives (figure 2). From the included studies 62 (64.6%) were original research studies and 34 (35.4%) non-original research studies (reviews, methodological papers, reports etc.)

Most frequent challenges highlighted by previous reviews were choice of modelling method, accounting for the clinical utility of the pCDx, lack of clinical trial data for the pCDx and the increased uncertainty related to the indirect impact of pCDx.

Majority of the original research studies (79.0%) utilized **traditional modelling methods** such as static state transition cohort models or decision trees. Several studies highlighted, that this preference may be due to their historical prevalence in the field, but they might not always capture the multi-faceted impacts of companion diagnostics effectively.

In contrast, only seven studies (11.3%) employed **more advanced simulation methods,** such as discrete event simulation or microsimulation. Reasoning for a specific modelling method was seldom provided.

Sensitivity and specificity (i.e., accuracy) of the companion diagnostic was considered in 25 studies (40.3%) and only 14 studies (22.6%) considered the **adherence to the pCDx recommendation.**

Lack of clinical trial data for pCDx clinical utility was the most common challenge regarding evidence gaps. Only 12 studies (19.4%) used data derived from clinical trials for pCDx clinical utility.

Increased uncertainty regarding pCDx economic evaluation results was identified in several studies, however only 32 studies (51.6%) addressed this by conducting comprehensive deterministic and probabilistic sensitivity analyses.

Fig. 1 PRISMA flow diagram

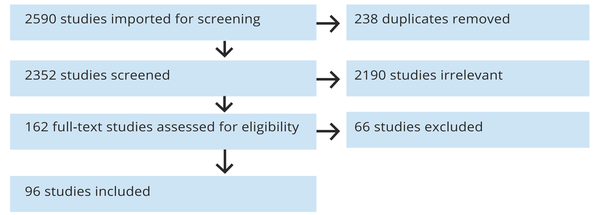
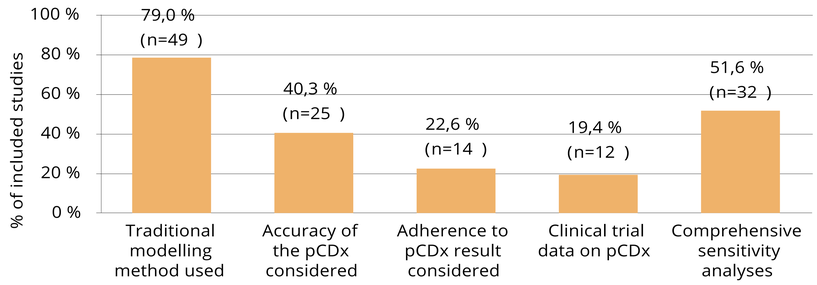


Fig. 2 Summary of key considerations in original research studies (n=62)



CONCLUSIONS

Future research should focus on addressing the most prominent challenges encountered in the economic evaluation of pCDx:

1. Develop guidance on selecting the most suitable modeling method to effectively capture the intricate and multifaceted aspects of pCDx
2. Offer practical solutions for effectively incorporating the clinical utility of pCDx into economic evaluations when clinical trial data on pCDx is not available
3. Advocate for more robust sensitivity analyses, providing decision makers with a more thorough understanding of the uncertainties associated with pCDx

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Increasing prospects of radiomics artificial intelligence in breast cancer treatment planning

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