Challenges of Health Economic Evaluations Alongside Innovative Clinical Trial Designs in Precision Oncology – Results of a Literature Review

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Research for a Life without Cancer

Background

Research advancements in cancer care are rapidly moving towards precision oncology with targeted and personalized treatments. Innovative therapies are assessed in new types of clinical trials, such as adaptive, basket, and umbrella designs, focusing on specific genetic mutations independent of the cancer site. Yet, health economic evaluations still generally apply histology-based stratification of patients. Therefore, traditional health economic evaluations face difficulties while generating supportive evidence for health policy decision making alongside innovative clinical trials.

Objectives

This comprehensive literature review aims to synthesize the published evidence on these challenges and to provide an incentive to discover potential solutions.

Methods

A comprehensive literature search was conducted in PubMed on September 9, 2021. A search string constructed from terms describing relevant clinical trial designs, precision medicine, and health economic evaluations was used, restricted to challenges or issues around the economic analyses. All English-language studies that addressed methodological considerations for health economic evaluations of innovative clinical trials in precision medicine were included. References of relevant systematic reviews were searched to identify additional records.

Key results

The database search yielded 241 hits, and additional 5 studies were found by reference screening. Ten studies met the inclusion criteria for the qualitative synthesis. *(PRISMA flow chart is available on request.)*

Methodological challenges were extracted and categorized under the aspects of choice of perspective, time horizon, discounting, comparator selection, measurement of costs and health outcomes, and handling uncertainties and data gaps. The results of the literature review are presented here according to the main characteristics of health economic evaluations.

Perspective of the analysis

- Cancer is typically associated with high indirect costs, which are difficult to estimate in case of innovative therapies.

Time horizon

- Due to the high dropout rate, trial time horizons are particularly short.
- It is difficult to estimate either health outcomes or costs over a "sufficiently long" time horizon.
- Projecting outcomes is hindered by low patient numbers in the clinical trials.

Discounting

- Discount rates have a particularly significant impact on the results of the economic evaluation due to the high upfront costs.

Comparator selection

- Head-to-head comparison is often not available.
- The standard of care differs in clinical practice between cancer types.

Resource utilization and costs

- There are high upfront costs, such as genetic or biomarker testing.
- Long-term resource utilization and costs are uncertain and heterogeneous.
- Costs attributable to testing are unclear (i.e. no national lists).

Health outcomes

- Short-term surrogate endpoints in the trials might not capture relevant outcomes.
- There is a high dropout rate, often without follow-up.
- Patient heterogeneity might lead to different health benefits across cancer types and different quality of life of patients.
- Generalizability of observed health outcomes is limited.

Uncertainty

- Test characteristics, especially in the real-world setting, are challenging to estimate.
- Small sample sizes result in very wide confidence intervals.

Data gaps & data complexity

- Observational data and expert opinions are often the best available evidence.
- Genomic data is very complex and it is often unclear which of the multiple mutations is/are clinically relevant.
- Data on physicians´ and patients´ behavior and preferences is insufficient.

Conclusions and Discussion

Precision medicine has the potential to provide significant health benefits through therapeutic approaches tailored to individual patients. Yet, to gain market access and reimbursement, these innovative cancer treatments need to be evaluated by their clinical effectiveness and cost-effectiveness. New clinical trial designs bring several challenges while conducting health economic evaluations. Our literature review identified numerous challenges; however, the list of potential solutions is rather limited. Several issues arise from small study populations and short clinical trial time horizons in new trial designs, which hinder the robust assessment of clinical and cost-effectiveness. Challenges well-known to traditional cost-effectiveness analyses (e.g. estimating health outcomes) are also found to be amplified in the field of precision medicine. Further research is needed to explore how to conduct meaningful health economic evaluations alongside innovative clinical trials.

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