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HOW TO DEFINE THE VALUE OF ORPHAN DRUGS? A COMPARATIVE ANALYSIS OF VALUE ASSESSMENT FRAMEWORKS ACROSS EUROPE (EUROVAF)

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BACKGROUND & OBJECTIVE

Background: In order to assess the value of orphan drugs (OMPs), HTA bodies are exploring ways to capture aspects of value beyond those currently included in standard economic evaluation. Despite an increasing number of innovative decision-making - or 'value assessment' - frameworks being described in literature, decision-makers seem hesitant to adapt their HTA processes. **Objective:** This study aims to conduct a SWOT analysis of frameworks for the value assessment of orphan drugs from a theoretical perspective.

METHODS

Methods: A literature search was performed in scientific databases and policy documents to identify value assessment frameworks of OMPs. Publications were analyzed for strengths and shortcomings of each individual approach. Real-world experiences with frameworks in Europe were examined, as well as possible reasons for the lack thereof.

RESULTS

Table 1. Comparison of strengths and shortcomings of four value assessment frameworks for OMPs

	Strengths	Shortcomings
Standard economic evaluation	+ Equal treatment of OMPs vs non-OMPs. Currently no strong evidence for special treatment of OMPs based on prevalence +Manufacturers may better anticipate both risks and benefits before development and improve approaches to gather robust evidence when adhering to CE thresholds	– Less likely for OMPs to meet CE thresholds due to high uncertainty surrounding clinical efficacy and high price – Discussion on whether OMP legislation should warrant special reimbursement status for OMPs – Creates unequal access to treatment – A QALY ≠ QALY: not all QALYs are the same – QALYs do not capture all meaningful treatment effects – Issues with methods to elicit utilities – No consideration of societal preferences such as rarity, disease severity, unmet need
Weighing QALYs	+ Chance for reimbursement increases + More transparency surrounding inclusion of equity criteria such as disease severity	– Even if an OMP proves CE, feasibility due to their high price remains an issue – Does not reduce uncertainty of effectiveness – Societal preference studies, which determine criteria, contain flaws – Increases inequality when methodology is not legitimate – Higher complexity by attaching multiple attributes to QALYs
Variable ICER threshold	+Chance for reimbursement increases +More transparency surrounding inclusion of equity criteria such as disease severity	– Even if an OMP proves CE, feasibility due to their high price remains an issue – Does not reduce uncertainty of effectiveness – Societal preference studies, which determine criteria, contain flaws – Increases inequality when methodology is not legitimate – Higher threshold stimulates unnecessary risks and less cost-effective OMP development
MCDA	+ Flexibility to in- and exclude criteria + Weighing of criteria supports trade-offs between competing values + Structured decision-making by visualizing criteria +Increased transparency as key decision-making arguments become traceable + Multi-perspective interpretation of evidence + Legitimacy & acceptability of final decision + Data uncertainty is managed accordingly + In time: more consistency between appraisals insight into (country specific) societal preferences investments directed towards criteria with higher value	– Does not reduce uncertainty of effectiveness – Complicates effective budget-management if BI considered less important – Issues with overlap, interdependency and invalidity of criteria in complex decision-making context – No consistency between current frameworks – No benchmark for comparison of composite scores – Reluctancy towards transparency

CONCLUSION

The frameworks listed above each have their strengths and weaknesses, yet none of them is perfect. All share the same shortcomings: **they do not reduce uncertainty of data nor do they manage feasibility of funding**. These shortcomings complicate, yet do not prevent a decision from being made. As such, **any tool(s) addressing these issues can be developed independently of a decision-making framework**. For uncertainty, such tools may include disease-specific registries, value-of-information techniques or MEAs focused on evidence generation. For feasibility, suggestions include additional dose-response studies, risk-sharing agreements or rate-of-return pricing for cost-ineffective OMPs, which are still believed to provide significant value for patients. Finally, **none of the frameworks provide the ultimate valid approach for the inclusion of societal preferences.** However, MCDA does allow the incorporation of these preferences in such a way that they can be considered deliberately by multiple stakeholders. Moreover, as preference studies improve over time, the framework allows their further in- or exclusion and an *ad hoc*, yet legitimate adaptation of their respective weights. As such, **MCDA seems to provide what is most important in any ethical decision-making framework for OMPs. That is, the legitimacy of the trade-offs between competing efficiency and equity values, through transparency surrounding criteria, their weights and the involvement of multiple stakeholders.**

Abbreviations: BI: budget impact; CE: cost-effective; HTA: health technology assessment; ICER: incremental cost-effectiveness ratio; MCDA: multi-criteria decision analysis; MEA: managed entry agreement; OMP: orphan medicinal product; QALY: quality-adjusted life year; SWOT: strengths, weaknesses, opportunities and threats