ADAPTING GLOBAL COST-EFFECTIVENESS MODELS:

KEY CHALLENGES, RECOMMENDATIONS, AND FUTURE DIRECTIONS

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Understanding the adaptation of global cost-effectiveness models

Cost-effectiveness models (CEMs) are essential tools in health technology assessments (HTAs), providing evidence to demonstrate the economic value of new healthcare interventions in countries that use economic evaluations to inform reimbursement decision of such interventions.[1] HTA enables countries to rigorously evaluate the clinical and economic "added value" of new interventions before authorizing market access and reimbursement, making CEMs a critical component of the submission package. Generally speaking, pharmaceutical companies will develop a core "global" CEM suitable for local adaptation by affiliate countries; therefore, each country does not have to start from scratch. Countries that launch later, such as those in South America, Asia-Pacific, and the Caribbean, usually adapt existing global CEMs for their local market, for efficiency and consistency.[1,2] The stakeholders from these regions choose to utilize HTA reports from the United Kingdom and European countries, the United States, Canada, and Australia due to the applicability of the description, and the proven safety and efficacy of the technologies discussed.[3] Adapting a global CEM across different countries to enable region-specific economic assessments of interventions requires modifying the original model's structure to reflect the relevant demographic, economic, and clinical features of the target country. This includes local population estimates, disease and mortality rates, risk factors, direct and indirect costs, available treatment options, discount rates, cost-effectiveness thresholds, and perspectives. In this article, we will explore the key challenges and recommendations associated with adapting global CEMs, along with perspective on future directions.

Key challenges and recommendations associated with adapting global cost-effectiveness models

Challenge	Recommendation
***Sparse or Incomplete Data for Resource Utilization and Unit Costs*:** There is often sparse or incomplete data for resource utilization estimates and unit costs specific to the local context to estimate the total costs related to treatment and management in a particular therapeutic area. For example, in the context of direct costs, resource utilization and unit cost data specific to emergency department and outpatient visits are often not publicly available. In addition, information regarding indirect costs (e.g. caregiver work loss days, income, travel) are often not publicly available.	Execute regional costing studies and/or include key opinion leaders for elicitation of clinical expert and real-world knowledge.
***Sparse or Incomplete Epidemiology Data*:** There is often sparse or incomplete data at the country or local level, such as the frequency of the disease and disease-specific mortality rate, which are often difficult to obtain	Apply values from a global systematic review and/or include key opinion leaders for elicitation of clinical expert and real-world knowledge.
Critical Demographic Data Not Available: Critical demographic data such as exact population estimates are often not publicly available. For example, it may be difficult to source the most recent estimates for the number of people who live in certain regions/countries or fall into specific age categories.	Apply relevant, conservative, and transparent assumptions based on the available public data, or identify appropriate proxy geography to apply. State methods clearly in model documentation.
Incomplete Data for Uptake of Interventions: There is often incomplete data for uptake of new interventions by disease status and/or age group.	Assume the uptake based on the timing of country-specific implementation of similar novel interventions historically. Enquire if the local affiliates have conducted a study to estimate market share infiltration of the new intervention. In the absence of uptake data stratified by disease status/age, assume equal uptake for all groups.

Key challenges and recommendations associated with adapting global cost-effectiveness models

Challenge	Recommendation
Viewing and Programming Restrictions Within the Global CEMs: Lack of transparency from the global organization for affiliates, including viewing and/or programming restrictions can hinder the implementation of necessary modifications for regional adaptations of the global CEM. For example, it may be difficult to view or change the background calculations for certain parameters in the model, making it difficult to understand or make adjustments relevant for the local setting.	Engage early communication with global modelling teams to obtain open-access to the model; provide clear guidance on model assumptions and inputs including which must be modified at the local level.
Inability to Understand Data Sources Due to Language Barrier: There is often difficulty in accessing or interpreting some of the potential data sources due to the language barrier. This also means that some useful data sources could be potentially missed in the process of data collection.	Include local affiliates with knowledge of the local language.
Lack of Reliable Utility Data: There is often a lack of reliable country-specific utility data stratified by age or disease groups.	Apply utility values as per a nearby country or region.
Lack of Economic Evaluation Guidelines: A lack of formal economic evaluation guidelines for HTA submission requirements is problematic in the context of choosing the correct perspective, discount rates, and cost-effectiveness threshold.	Conduct a targeted review and analysis on previous regional reimbursement decisions; this can help to provide a framework for HTA submissions.

Future directions in adapting global cost-effectiveness models

Possible role of artificial intelligence (AI)

Recent position statements from the National Institute for Health and Care Excellence (NICE) and Canada's Drug Agency (CDA) outline a range of promising applications for AI and machine learning in health economic modelling.[4,5] These technologies could be used not only to assist with model development, validation, and reporting but also to analyze complex datasets, automate updates, and improve the efficiency of simulations.[4,5] As these capabilities continue to evolve, early research, including two recent studies on large language models (LLMs), offers insight into how AI might be applied to streamline certain processes in CEM adaptations.

Two recent ISPOR publications (a poster and a podium presentation) by Rawlinson and colleagues (2024) have discussed the capabilities of GPT-4 in automatically adapting a global technical report (built in Microsoft Word) and CEM (built in Microsoft Excel) to a country-specific setting.[6,7] It is important to note that only the results and discussion section of the report were updated using an LLM, while technical reports usually also contain introduction, methods, and inputs sections. The findings showed that accuracy was 94.3% for the AI-generated report and 97.1% for the manually adapted report. Regarding the potential of generative AI in automatically adapting CEMs, it is important to mention that the adaptation by Rawlinson and colleagues (2024) was restricted to editing input values only, while country-specific data were collected from the literature previously by the personnel team. The findings showed that the AI-generated adaptations were performed in 245 seconds with 97% accuracy, and that GPT-4 performed 62 out of the 64 required updates.

Conclusion

The article has characterized challenges and associated recommendations for adapting global CEMs to other countries of interest. Implementation of these recommendations will allow manufacturers to improve the quality and credibility of global CEMs adapted for the local context and increase the likelihood of launch success. Finally, AI is emerging as a promising area for CEM adaptation, with early evidence suggesting its potential to automate and enhance certain processes involved in adapting global CEMs, though human oversight remains critical to ensure accurate, robust, and contextually appropriate outputs and interpretation of results.

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