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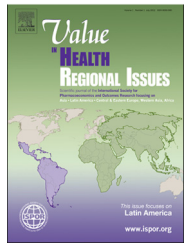

Guidance Document: Global Pharmacoeconomic Model Adaption Strategies

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ABSTRACT

Objective: The purpose of this guidance was to assist in the adaptation of pharmacoeconomic models originally developed in one country and intended for use in another. The intent was to produce user-friendly recommendations and a checklist for adapting a global model to treat a specific disease state. This guidance will allow model developers to tailor existing models so that they are "locally applicable," while maintaining the scientific integrity of the original pharmacoeconomic model and will benefit formulary decision makers and other stakeholders involved in evaluating pharmacoeconomic studies. **Methods:** A working group of experts from various countries participated in the Global Pharmacoeconomic Model Guidance development to discuss the adaptation of pharmacoeconomic models. A systematic review of studies adapting pharmacoeconomic models and translation across countries was conducted and recommendations were made for adaptation. The working group interviewed internal and external stakeholders to solicit best practices for model adaptation and developed a draft set of key principles and general recommendations for global adaptation. **Results:** The working group provided a set of 16 recommendations for adapting pharmacoeconomic models for local decision makers. The recommendations span various aspects of estimating or modeling both the costs and effectiveness of pharmacoeconomic models as well as guidance for ensuring local acceptability. **Conclusions:** These recommendations and the related principles not only will provide pharmacoeconomic models that are meaningful to local decision makers but also will improve the consistency and credibility of pharmacoeconomic model adaptations. The guidance may also help those who will build the original models to design them with the flexibility to allow pharmacoeconomic model adaptations as described in this document.

Keywords: cost-effectiveness analysis, health technology assessment, pharmacoeconomic model.

Introduction

Economic modeling is widely used in economic evaluation of pharmaceuticals (cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis, and budget impact analysis) to evaluate the health care costs and health outcomes of alternative courses of action in the presence of scarce resources in terms of both their cost and consequences. A number of countries faced with increasing pressure to make use of health care resources use economic evaluations to guide their reimbursement of pharmaceuticals [1,2]. For example, Latin America and Caribbean stakeholders need to adapt existing pharmacoeconomic models for the local region. They need to consider coverage and reimbursement, as well as clinical decision making. These stakeholders prefer to adapt health technology assessment reports from Europe, the United States, Canada, and Australia because of the applicability of the description, as well as the safety and effectiveness of the technology [3]. The adaptation of a pharmacoeconomic model across different countries to support region-specific economic evaluation of pharmaceuticals requires the originally developed model to structurally adapt to the economic and clinical characteristics of the intended country. Ensuring the reliability (i.e., reproducibility) of measurements across different geographical regions requires comparing and/or adjusting data from clinical trials, observational studies, claims databases, case registries, public health statistics, and surveys to estimate the economic impact of the uptake and use of a particular pharmaceutical in the intended country of interest.

The concept of "pharmacoeconomic model adaptation" raises the issue of "transferability" across geographical regions. The transferability of pharmacoeconomic models refers to the adaptation of

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clinical effectiveness and cost-effectiveness data across geographical regions [4]. The transferability of economic evaluation results requires the use of a general "knockout criteria" to determine whether the model can be transferred to the decision country [2]. To ensure the reliability of the pharmacoeconomic model, the analyst must then determine which part(s) of the model needs to be adapted to reproduce the model in a different geographic region. To determine which parts of the model need adaptation, there are several transferability factors to consider.

The factors that create challenges for developing a model for adaptation include differences in the epidemiology of the disease, mortality rates, disease severity, demographic characteristics, risk factors, available treatment options, discount rates, absolute or relative prices, and differences in practice patterns [5–8]. These factors can be broadly grouped into methodological, health care system, and population characteristics [7]. The transferability of the above factors or of the entire pharmacoeconomic model will depend on the type of economic modeling, data availability, and the need for modeling-based adjustments. For example, if the goal of the pharmacoeconomic model is to measure the economic burden of a disease or diseases on a particular society in monetary terms, it is important that costs and effects accruing in future years be discounted to their present value using widely accepted rates because the time horizon for therapies in certain conditions is long [5,9]. This is especially true for chronic diseases—such as heart disease, cancer, and diabetes—in which the course of the disease is persistent or long-lasting in nature. However, because the perspective of the decision maker is usually the societal perspective for resource allocation decisions, the choice of a discount rate for economic evaluation may not reflect the societal preference for the intended country. When there is variability in the discount rate, the appropriate societal discount rate should be chosen on the basis of the perspective of the analysis and on some theoretical approach, especially when the analytic result is sensitive to the discount rate [6]. Although the choice of the discount rate is an important topic in the context of health economic evaluations, we must also underscore the importance of relative prices.

It is recommended that pharmacoeconomic models include all relevant direct health care costs in the evaluation, including indirect costs when appropriate, which will depend on the aim of the study, treatment comparator, the perspective of the evaluation, and the guidelines of the jurisdiction [10]. Unit cost prices of pharmaceuticals and/or medical services should be from the jurisdiction of interest, but due to possible differences in relative or absolute prices, the data on resource use may need to be adapted to the jurisdiction of interest [3]. Currently, there is no consistent guidance on how to address the transferability of economic data for evaluation or on how to adjust for such differences in prices between jurisdictions [3,11]. Addressing the differences in relative prices is very important for determining what happens to the transfer of economic data from one country to another because these differences can lead to different interpretations of cost-effectiveness data in the jurisdiction of interest, especially if there are substantial differences in relative prices [3,11,12]. The comparison of prices across jurisdictions has been the subject of careful investigation of whether markets are truly integrated [13], a term used to describe how much different markets are to each other. There is evidence to suggest that countries/jurisdictions within geographic proximity, similar health care structure, and/or similar political economy will likely have cost-effectiveness results that are generalizable [10,14,15]. This idea of prices of similar products to be equal across countries is especially true for countries within the European Monetary System, which operate under a unified currency, the euro. The use of purchasing-power-parity exchange rates or market exchange rates in economic modeling may be necessary when there exist some widely varying price structures between countries; the latter is likely to provide inaccurate estimates of relative incomes and outputs [16].

Difference in medical practice patterns across geographic regions is another important factor to consider when transferring cost-effectiveness data to another jurisdiction. These differences in medical practice between countries would produce differences in resource input, utilization of services, and expenditure among neighboring jurisdictions [17]. Therefore, practice variations between countries/jurisdictions are likely to cause uncertainty in the apparent effectiveness of the health service and thereby make the transferability of cost-effectiveness estimates from one country to another impractical unless adjustments can be made [11,18]. Adjustments for differences in medical consumption on relatively homogenous groups can be done by correcting for the difference either upward or downward [11].

In determining the transferability of clinical and economic data, pharmacoeconomic models must also address another important factor known as the *case mix*. A case mix is composed of subgroups of patients possessing similar demographic characteristics, clinical attributes, and output utilization patterns [19]. A case mix–based payment system assumes that within diagnosis-related groups there is little variability in clinical attributes and processes of care; therefore, the cost-effectiveness results can be transferable across jurisdictions with similar case mix. Case-mix differences can account for higher medical cost [20], differences in medical treatment practices [21], and variations in treatment outcomes [22] in certain jurisdictions. Variation in treatment outcome is termed "heterogeneity of treatment effects" and identifying potential heterogeneity of treatment effects is necessary to aid in the design of pharmacoeconomic model for adaptation. The type or mix of patients treated may vary substantially between countries, which can affect the cost-effectiveness of an intervention. Therefore, if the heterogeneity of treatment effects in certain jurisdictions is likely, then the use of statistical methods may be needed to adjust for observed differences, and thus allow for more (less) specific therapeutic recommendations in the jurisdiction of interest [23–26].

Methods

A working group was convened consisting of experts from various countries who participated in a Global Pharmacoeconomic Model Guidance development to discuss the adaptation of pharmacoeconomic models, originally developed in one country for use in another country. A review of studies adapting pharmacoeconomic models and translation across countries was conducted. The working group discussed controversies surrounding "translation" across countries and recommendations to consider for adaptation. Before preparing the draft report, the working group interviewed internal and external stakeholders responsible for conducting modeling studies to solicit best practices for model adaptation. The Global Pharmacoeconomic Model Guidance working group developed a draft set of key principles and general recommendations for global adaptation. The working group met by phone 4 times and used a Delphi approach via e-mail to obtain consensus on the final set of recommendations. Each working group member was also asked to obtain input from two or three additional experts from his or her region. Based on solicited feedback on these draft recommendations, a set of final recommendations and corresponding rationale was developed.

Results

The research results described in this guidance define acceptable standards and explains best practices for the transferability of economic and clinical data before submitting an economic evaluation for reimbursement. It takes into account the accepted hierarchies in the levels of evidence (see Fig. 1) and also provides pragmatic recommendations. A checklist (see Fig. 2) is provided at