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 formulation 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...
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 homogeneous 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
the end of the document to guide those who implement pharmacoeconomic model adaptations.

Recommendation 1: When adapting a pharmacoeconomic model for local decision makers, follow recommendations for good research practices for conducting pharmacoeconomic studies and pharmacoeconomic modeling, such as those provided by ISPOR.

Rationale: Local adaptation of a pharmacoeconomic model assumes that the original model is methodologically sound. Otherwise, the adaptation will retain the same flaws that were inherent in the original pharmacoeconomic model.

Implementation: Before adapting a model, the original model should be vetted by at least three experts for structure and scientific integrity if that was not done during the original pharmacoeconomic model development process.

Recommendation 2: Familiarize yourself with national, regional, local, or individual payer or technology appraisal agency pharmacoeconomic guidelines and use recommendations and suggested best practices when adapting a global model for individual payer decision makers.

Rationale: National or local pharmacoeconomic guidelines developed by jurisdictional experts reflect the best judgment on pharmacoeconomic practices and strategies of pharmacoeconomics in the context of their jurisdiction. Many of these guidelines are consensus documents developed by multiple stakeholders and experts working within the country even if they are not officially endorsed by a government entity. After extensive research and evaluation, the opinion leaders in the country propose their expert opinion on the most effective pharmacoeconomic practices for the country, and such experts often influence the appraisal or coverage decision processes. Thus, such guidelines should be followed when they exist, even when they are in conflict with other recommendations contained in this guidance. A sensitivity analysis, however, may be warranted to reflect the recommendations contained herein to provide scientific validity and because guidance documents may evolve over time.

Implementation: Before submitting an economic evaluation for reimbursement, determine whether there are guidelines that represent a consensus view among economists and experts in the intended country of interest. If no such guidance exists, consider regional guidelines and/or recruiting a local expert and/or key opinion leader from the region to review the adaptation process and resulting pharmacoeconomic model to ensure credibility and applicability.

Recommendation 3: Determine the perspective of the adaptation, which may be a societal national payer, a regional payer, or an institutional perspective. The perspective will determine other aspects of pharmacoeconomic model adaptation.

Rationale: The societal perspective is commonly used in cost-effectiveness analysis, but the choice of the study perspective should consider the decision maker regarding the use of new technologies in a particular country.

Implementation: In the absence of specific guidance from the local decision maker, provide both the societal perspective and a narrow focus on direct medical costs only. If desirable, also include an intermediate perspective (e.g., direct medical costs and productivity costs).

Recommendation 4: Select the comparators that reflect the current treatments and treatment algorithms (e.g., dose and duration) that are most likely to be replaced by the new therapy.

Rationale: The choice of the appropriate comparator is very critical because the cost-effectiveness of an intervention is a relative measure of the cost and effectiveness of any alternative, which is dependent on the choice of the comparator.

Implementation: The choice of the comparator must be appropriate to the research question and should reflect current practice or the most widely used therapy/therapies in the jurisdiction of interest. Occasionally, current practice may differ by jurisdiction, so the payer or decision maker in the jurisdiction of interest may specify which alternatives should be compared.

Recommendation 5: Always use cost data from the specific country. When various data sources exist, the following data hierarchy should guide which data source is most reliable and applicable for pharmacoeconomic model adaptations for cost or resource utilization estimation: 1) national estimates, 2) regional/local estimates, 3) single or group of hospitals or institutions, and 4) expert opinion.

Rationale: The geographical separations of markets, differences in clinical practice patterns, different payment systems, and various incentives from drug manufacturers are some of the various factors identified as preventing prices of similar products to be equal across countries or variability in resource use between locations. The international markets are not as integrated as domestic markets, so it is important that national estimates data for resource consumption be considered first.

Implementation: If cost data from the specific country are not available, apply a standard cost per procedure across all participating sites to derive a dollar value for costs of care.
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<thead>
<tr>
<th>No.</th>
<th>Recommendation</th>
<th>Implementation</th>
<th>Yes</th>
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<tbody>
<tr>
<td>1</td>
<td>Conduct good research practice for Pharmacoeconomic studies</td>
<td>The original model should be vetted for structure and scientific integrity.</td>
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<td>2</td>
<td>Use recommended economic appraisal guidelines and required reporting and appraisal standards</td>
<td>Refer to recommended economic appraisal guidelines. If no such guidance exists, consider recruiting a local expert and/or key opinion leader from the region to assure credibility and applicability.</td>
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<td>3</td>
<td>Determine perspective of economic appraisal</td>
<td>In the absence of specific guidance from local decision maker, use both the societal perspective and a narrow focus on direct medical costs only. If desirable, include intermediate perspective.</td>
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<td>4</td>
<td>Select available treatment options (comparators)</td>
<td>Use current practice or the most widely used therapy/therapies in the jurisdiction of interest.</td>
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<td>5</td>
<td>Consider the source of cost data</td>
<td>If cost data from the specific country is not available, apply a standard cost per procedure.</td>
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<td>6</td>
<td>Identify and quantify resource use and costs</td>
<td>Include relevant direct and indirect costs associated with the treatment. An activity-based costing method can generate a more accurate product costs.</td>
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<td>7</td>
<td>Consider clinical practice patterns and guidelines</td>
<td>When using decision analytic modeling, incorporate clinical practice patterns/guidelines of the intended country/jurisdiction of interest.</td>
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<td>8</td>
<td>Use country/region specific epidemiologic data</td>
<td>If country/region specific epidemiologic data are not available, use random-effect meta-analysis models and transition probabilities where necessary.</td>
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<td>9</td>
<td>Explain and justify use of estimated treatment effect</td>
<td>Use the average treatment effect from a multinational trial. Conduct a sensitivity analysis using treatment effect based upon patients from the specific country or region.</td>
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<td>10</td>
<td>Use health state preferences/utilities that are applicable to the region</td>
<td>Use local health state preferences and utilities whenever they are available; Use the average of published ones if local utilities are not available. If a revalidation is required/desired, include forward translation, back translation, and pretesting of the instrument.</td>
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<td>11</td>
<td>Utilize expert opinion sparingly and appropriately</td>
<td>Expert opinion represents lower levels of evidence. Whenever expert opinion is used, multiple experts should be involved. Use the Delphi method for consensus.</td>
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<td>12</td>
<td>Use modeling to address nontransferable elements</td>
<td>For data elements that are nontransferable, the model structure, data used as inputs to models, and model validation are important when assessing the quality of models. See <a href="http://www.ispor.org/taskforces/GRPMModelingTf.asp">http://www.ispor.org/taskforces/GRPMModelingTf.asp</a> for more information.</td>
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<td>13</td>
<td>Utilize quality-adjusted life years(QALYs)</td>
<td>Determine threshold to enable transfer and applicability of QALYs across jurisdictions unless local guidelines recommend a different metric or approach.</td>
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<td>14</td>
<td>Determine and justify discount rate</td>
<td>Use local guidance for discount rate. If none exist, use a “real riskless” discount rate of 3% and conduct sensitivity analysis.</td>
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<td>15</td>
<td>Source and justification of each data element in PE model</td>
<td>To reflect an evidence-based approach to PE modeling, systematic reviews of the literature should be conducted.</td>
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<td>16</td>
<td>Translate findings for the desired perspective</td>
<td>The perspective, the recommendations concerning evaluation of resource use/costs, the choice of the comparator, and the valuation of costs should be considered before considering the transferability and reproducibility.</td>
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**Fig. 2 – Checklist of pharmacoeconomic model adaptation strategies: A tool for decision making.**

Whenever expert opinion is used, multiple experts should be involved and ideally a Delphi process should be used to achieve consensus. **Recommendation 6:** Cost data should include direct medical costs as well as other components of costs (e.g., lost productivity and overhead costs) when available from the specific country.
Costs should be disaggregated so that payer decision makers are able to determine where the components come from and which costs are the major drivers.

Rationale: Many factors affect medical care costs, and the disaggregation of cost into individual cost drivers can uncover the major source of variation in medical care costs from one jurisdiction/region from another.

Implementation: In cost estimation procedures, assigning cost to cost out products may require including other components of costs on a cause-and-effect-basis. An activity-based costing method with multiple cost pools, activity drivers, and allocation bases can generate more accurate product costs.

Recommendation 7: Incorporate clinical practice patterns that reflect how the disease or condition is treated within the jurisdiction. In doing so, be sure to address whether treatment occurs at a hospital, an outpatient clinic, or a physician office. Also address the number and types of drugs, other health technologies, and services received, including whether general practitioners and/or specialist physicians are involved in treatment.

Rationale: Differences in medical practice patterns between countries can produce differences in resource input, utilization of services, and expenditure among neighboring jurisdictions, thereby causing uncertainty in the apparent cost-effectiveness of the health service.

Implementation: Understand and incorporate the patterns of clinical practice or clinical guidelines in the intended country/jurisdiction of interest when using statistical techniques such as Markov analysis, decision trees, and discrete event simulation to extrapolate results from one jurisdiction to another.

Recommendation 8: Use country-specific incidence or prevalence and other local epidemiologic data (e.g., clinical parameters, mortality, morbidity, and comorbidity) and transition probabilities when adapting a pharmacoeconomic model, even if treatment patterns are similar to the practice of medicine in the original model’s country.

Rationale: Even if the baseline risk of disease is the same across countries, the progression of disease could differ, so local transition probabilities between health states may differ from those within the original pharmacoeconomic model.

Implementation: Use Markov transition models to model disease progression. Transition probabilities should reflect the current health state of persons in the intended country of interest and not the health states of those in the original model. If country-specific incidence or prevalence rates and other local epidemiologic data are not available, use random-effect meta-analysis models to combine the evidence data and then convert into transition probabilities if necessary; in such instances, sensitivity analysis is recommended.

Recommendation 9: In contrast to other aspects of a pharmacoeconomic model, the treatment effect generally is highly transferable and, therefore, often does not need to be altered during country adaptation. Therefore, if adaptations are made, justify why the treatment effect is tailored and provide a valid source for the local data on the effect of treatment.

Rationale: Unlike estimates of baseline risk, estimates of treatment effect are generally considered to have high transferability when there is little to no difference in patient characteristics, comparators, and treatment practice patterns.

Implementation: In addition to using the average treatment effect from a multinational trial, the treatment effect based on patients from the specific country or region should be provided as sensitivity analysis unless the sample size is extremely small.

Recommendation 10: Health state preferences/utilities are not transferable; therefore, a study-specific evaluation is needed to obtain local values for such data elements. Unless such estimates are obtained through a valid patient-reported outcome (PRO) instrument (including linguistic validation), it is preferable to use a published or otherwise validated estimate from another jurisdiction.

Rationale: Health state utilities quantify an individual’s preferences for different health outcomes and so the use of an existing validated PRO instrument does not necessarily enable the transfer of preferences/utilities across different countries/jurisdictions to predict preferences associated with actual experienced health states. Therefore, to reflect a more valid preference associated with an experienced health state in the country/jurisdiction of interest, translation and cultural adaptation of existing instrument is recommended. The average of published utilities, however, can be used if local utilities are not available.

Implementation: Use local health state preferences and utilities whenever they are available; however, if local utilities are not available, use the average of published ones along with sensitivity analysis. If a revaluation of a PRO is required/desired, the process should include forward translation, back translation, and pretesting of the instrument to assess the PRO.

Recommendation 11: Country-specific data are generally preferred over local expert opinion when available. The balance between country-specific data and expert opinion is a spectrum. The more data that are available, the less expert opinion is necessary, while a lack of data must be supplemented with expert opinion. Expert opinion should be used to evaluate the quality of the data and the ability for it to be transferred to the specific country.

Rationale: Clinical decision making and recommendations based on expert opinion represent lower levels of evidence, indicating little to no objective empirical evidence.

Implementation: As stated in Recommendation 5, whenever expert opinion is used, multiple experts should be involved and ideally a Delphi process should be used to achieve consensus.

Recommendation 12: Modeling can be used when key data elements are found to be nontransferable and should incorporate the demographic characteristics of the local jurisdiction.

Rationale: If the cost-effectiveness results of a treatment are not easily transferable from location to location, then random-effects meta-analysis models may be used to pool estimates and some form of formal modeling approach is needed.

Implementation: ISPOR and the Society for Medical Decision Making had a Joint Modeling Good Research Practices Task Force. The current draft of the series of reports is available online at http://www.ispor.org/taskforces/GRPModelingTf.asp.

Recommendation 13: Despite concerns about the estimation and transferability of utilities, quality-adjusted life-years (QALYs) remain an accepted “second best” metric and should be used as a primary output of pharmacoeconomic models across jurisdictions unless local guidelines recommend a different metric or approach.

Rationale: Population values and preferences could vary, but the QALY metric represents a generic outcome measure that can be applied more generally.

Implementation: The transfer and applicability of QALYs across jurisdictions will be largely driven by the threshold value for the QALY, the use of an utility instrument that ensures that concepts within an instrument are equal between original and target jurisdiction (language, time, and context), and the appropriateness of the instrument for assessing utility.

Recommendation 14: Use a discount factor that reflects the appropriate discount rate for the local jurisdiction.

Rationale: The perspective of the decision maker is usually the societal perspective for resource allocation decisions. The choice of a discount rate for economic evaluations should reflect the societal preference for the intended country because an analytic result can be sensitive to the discount rate.

Implementation: If there is local guidance for a specific discount rate, use that rate. If there is no local guidance, use a “real riskless” discount rate of 3% and sensitivity analysis using 5% as well as a reasonable range of discount rates (e.g., 0%–10%).
Recommendation 15: Provide a source and justification for each data element or assumption that is included in the adaptation so that the pharmacoeconomic model adaptation clearly reflects an evidence-based approach to pharmacoeconomic modeling; also, justify why parameters that are kept from the original model are not changed.

Rationale: The transparency of methods and justification of key parameters in the model will not only ensure transferability and reproducibility of results but would also influence the allocation of health resources by decision makers.

Implementation: Conduct a systematic literature review to provide inputs for the economic model. Regularly, sources such as “previous unpublished study” or “presentation on a local conference” are used to retrieve input data. In particular in small countries with missing national literature sources, such inputs may be inherited for years.

Recommendation 16: Provide a translation of findings that addresses the perspective of the local decision maker so that results are believable and meaningful.

Rationale: The guidelines for health economic evaluations generally point out that the perspective should be the societal perspective. The choice of the analytical aspects of the study should be within the scope of the perspective.

Implementation: Guidelines for health economic evaluations may vary between jurisdictions and so the perspective of the evaluation, the recommendations concerning the evaluation of resource use/ costs, the choice of the appropriate treatment comparator, and the valuation of costs should be considered before considering the transferability and reproducibility of the study results.

Conclusions

The following key guiding principles should be kept in mind to guide pharmacoeconomic model adaptations across geographic jurisdictions.

Principle 1: Before developing a local adaptation of a model, the model and availability of data should be evaluated using general knockout criteria or a checklist of critical transferability factors. A minimum standard of quality must be met before the local adaptation can even be considered for transferability [7,27].

Principle 2: Throughout this document, the term “local” jurisdiction is used to describe the jurisdiction or institution for which a pharmacoeconomic model is being adapted and, as such, could reflect a country, a region within a country, a specific national, regional, or local payer, a single institution, or a group of institutions. Assess the variability of the factors that can potentially affect the transferability of data from one “local” jurisdiction to another and perform probabilistic or multivariate sensitivity analysis [8,11,28,29].

Principle 3: Transferability is a spectrum, with “fully transferable” data describing a model that is completely transferable across a group of countries or jurisdictions with similar health care environments and pharmacoeconomic practices. “Nontransferable” describes a situation in which there is a critical failure that makes the entire model nontransferable either because of the model structure or data availability in the local jurisdiction. Within a study deemed to be transferable, each data element also exists on a spectrum of transferability [5,8,30].

Principle 4: A well-constructed model that is designed with adaptation in mind often is transferable across a wide area of countries. Frequently, the problem with adaptation is not so much the structure of the model so much as the lack of data availability for the adaptation process. The model structure is more problematic when specific comparators or components of treatment are “hardwired” into the model structure; when that is the case, the model cannot be adapted to local decision makers for whom the comparator treatments or aspects of care do not apply [14,31].

Principle 5: Following the decision on whether part(s) or the whole model is deemed to be transferable, transparency of model assumptions, characteristics, and limitations for data elements that are considered transferable will allow economic evaluations to be more informative for the intended user in the decision-making process [10,32].

Principle 6: Before adaptation, the individual(s) who is responsible for tailoring the model must be trained on the model, ideally by the developer of the original model. This ensures that the local adaptation maintains the general structure and key components and properties of the pharmacoeconomic model [22,33].

Principle 7: Local adaptation is best informed with input from local decision makers or their proxies/surrogates in advance of model adaptation [34–36].

Principle 8: Countries differ in terms of whether they view pharmacoeconomic models to be transferable from countries that are either within their geographic proximity and/or have a similar health care structure. Political, social, and economic factors also affect whether a pharmacoeconomic model is transferable across jurisdictions. Before pooling data, the transferability between jurisdictions should be viewed as acceptable by the intended user of the pharmacoeconomic model. For example, transferability is viewed as reasonably acceptable among countries in Latin and South America that have similar size and economies and generally not acceptable among Asian countries. In Europe, transferability of effectiveness parameters is acceptable across Western and parts of Eastern Europe, whereas costs are not [21,37,38].

Principle 9: Countries that have limited experience with pharmacoeconomic evaluation and limited data availability are more likely to deem economic evaluations and data elements to be transferable. They also, however, are more likely to focus on affordability and so the pharmacoeconomic model may be less impactful than a budget impact model [24,39].

Principle 10: Despite advances in the use of pharmacoeconomic models and improvements in pharmacoeconomic modeling and adaptation, there is continued need for knowledge dissemination and efforts to increase awareness of local decision makers, which may include education of clinicians as well as policymakers because clinicians affect the policymakers’ decisions [24,40,41].

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