# CHAPTER 1

## Principles and methods

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# USING COST-EFFECTIVENESS RESULTS FROM ABROAD FOR LOCAL POLICY DECISIONS

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Healthcare professionals are under increasing pressure to manage the economic impact of pharmaceuticals. Economic data is often requested in support of decision-making procedures for their pricing and/or reimbursement. The authors look at the factors which affect the transferability of such data.

Decision makers and healthcare professionals, such as hospital pharmacists, are under increasing pressure to understand and manage the health consequences and economic impact of pharmaceuticals that are new to a healthcare market [1]. A growing number of jurisdictions request economic data in support of their decision-making procedures for the pricing and/or reimbursement of pharmaceuticals [2]. However, economic evaluations, of which cost-effectiveness analysis is the most commonly used method, are costly and time consuming which makes it not always possible to carry them out locally [3]. The increasing demand for cost-effectiveness analysis, limited research resources, time constraints and a shortage of evidence creates pressure to transfer data across jurisdictions [3, 4]. Some of the jurisdictions requiring data of economic evaluations in support of submissions for public reimbursement of pharmaceuticals have pointed out that the data need to be relevant to the local setting. However, little advice is offered on the approach to be adopted [5]. Unfortunately, economic evaluation findings, particularly costs, do not transfer well because of differences in healthcare and economic systems [6]. The transferability of economic evaluations is not only an issue between countries, but also within countries [7]. Therefore, decision makers commonly want conformation that a given economic evaluation is transferable to their particular population and treatment settings [8].

Although the concept of generalisability is related, it is regarded as something different. Generalisability is defined as the extent to which the results of a study can be generalised to the population from which the sample was drawn. Whereas, transferability is conceptualised as the extent to which the results of a study, as it applies to a particular setting, hold true for a different population or setting [9]. The results of an economic evaluation are transferable if potential users can assess whether the results apply to their settings and adapt them if necessary [3]. According to the ISPOR task force (2009) data are considered transferable if they can be adapted to other settings or jurisdictions [2].

It seems unrealistic to generate cost-effectiveness or cost-utility data for every decision-making context and therefore strategies for dealing with transferability issues need to be developed [5]. There are countless sources of variation to consider when adapting the economic evaluation results to a particular healthcare setting which, if not addressed, might lead to the inefficient implementation of new pharmaceuticals [1]. Even among countries with relatively similar healthcare systems there are differences in the results of economic evaluations [10]. For example, there are differences between neighbouring countries regarding the price of pharmaceuticals, variations in resource use or variation in the prescription and dosage of pharmaceuticals [11].

### PROBLEMS RELATED TO TRANSFERABILITY FACTORS

Transferability factors are factors that are likely to generate differences in economic evaluation results between settings or affect the transferability of economic evaluation data [12, 13]. Several factors have an influence on the differences between countries, which results in variation of the cost-effectiveness of pharmaceuticals from place to place [12, 14]. The factors can be classified into five different categories of characteristics, based on characteristics of the patient, the disease, the provider, the healthcare system and economic evaluation-methodology used. The following factors are often referred to: demographics of the population; epidemiology of disease; clinical practice; experience, education and training of the healthcare professionals; incentives for providers; absolute or relative prices (if the relative prices of pharmaceuticals differ between countries then the relative cost-effectiveness will also differ); available resources and services; organisation of delivery system; available treatment options (the so-called comparators in an economic evaluation); perspective of the economic evaluation and study factors [5, 13].

From this, it could be argued that the transferability of the results of an economic evaluation is influenced by a large variety of factors. However, there are three main factors that are commonly advocated when transferring data across jurisdictions: unit costs, resource utilisation or practice patterns,

and clinical efficacy [13]. Other important factors that have been mentioned are the availability of healthcare resources and population preferences [10]. It is widely expressed that there are sometimes substantial differences in unit prices across jurisdictions. Most researchers state that at least the unit prices need to be replaced when transferring economic evaluations. However, not only the differences in absolute prices are important, but also the relative price differences. Furthermore, there are sometimes important differences in clinical practice across jurisdictions, which can have a significant impact on the cost-effectiveness of an intervention [13]. All these differences should be taken into account when transferring economic evaluations across countries. Most research on transferability has focused on the costing side of economic evaluations. On the effect side, the EQ-5D is a frequently used instrument to measure health-related quality of life in economic evaluations, which was developed to compare the population preference health states across countries.

**Table 1: Steps for determining appropriate methods for adjusting cost-effectiveness information**

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|---|---|---|
| **Step 1** | | |
| Is the study of acceptable quality and relevant to the decision problem? (see [4]) ⇩ (yes) | ⇨ (no) | Consider collecting other data and/or modelling. |
| **Step 2** | | |
| Are the treatment patterns represented in the study similar to local treatment patterns? ⇩ (no) | ⇨ (yes) | Consider simple adaptation, e.g. applying local unit costs, using national health state valuation. |
| **Step 3** | | |
| Is the study based on data from a multi-location randomised trial? ⇩ (no) | ⇨ (yes) | Consider using statistical methods. |
| Develop a decision-analytic model. | | |

Based on ISPOR task force on transferability of economic evaluations across jurisdictions [2].

At the moment the EQ-5D has 17 country specific value sets which can be used to calculate the utilities for a specific health states [15, 16]. Nevertheless, utility estimates from foreign studies are often used directly for cost-effectiveness estimates, without adaptation by applying the appropriate national value set. However, recent research has indicated that using utilities obtained in one jurisdiction are often not equal to the valuation of health states of the general population in another jurisdiction, which can lead to misleading results. It is therefore not advisable to transfer utilities from one country to another without any adjustment [16].

## Possible solutions for using economic evaluations from abroad

For each evaluation it is necessary to define in advance a clear and appropriately specified decision problem. This requires a description of the patient population and the comparators to the new technology. It is possible that a specified decision problem related to new pharmaceuticals varies between jurisdictions. The first reason is that licences can differ between countries and this can affect the clinical applications of the new product, or of the comparators. A second reason relates to the differences in treatment patterns, where interventions used in one country are not used in another, which affect the choice of comparators [2].

## Assessing the transferability of economic evaluations

A checklist was developed by Boulenger et al. comprising 42 questions and a sub-checklist of 16 questions, which assesses the level of reporting of transferability information [17]. For each question the answers are classified as: 'yes', 'partially', 'no/no information provided' or 'not applicable'. The responses are given the following score: 1 for 'yes', 0.5 for 'partially' and 0 for 'no/no information'. When the response to a question is 'not applicable', the question is excluded from the scoring by reducing the denominator accordingly. A summary score can be derived using the following formula: $1/n\text{-}x\ \Sigma_i\ S_i * 100$, where n = number of questions, x = number of questions with the response 'not applicable' and S = score for each question. The answers to the questions lead to a transferability information score. Boulenger et al. reported a mean score of 66.9 ± 13.6% and the scores on the checklist and the sub-checklist, which focus specifically on transferability, were comparable. However, no standard is available and therefore it is difficult to determine what a score indicates [17].

## Transferability of decision-analytic models

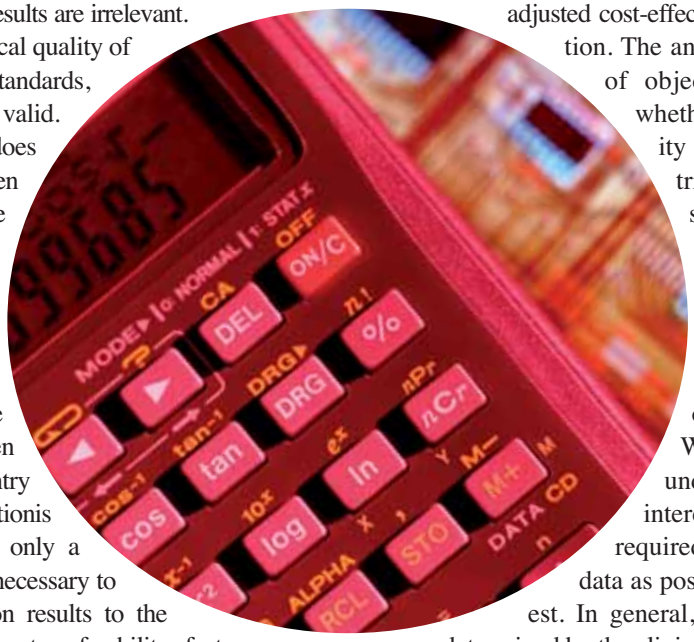
An assessment of the transferability of decision-analytic models can be carried out by paying attention to four particular topics [18]. These topics were chosen to assess whether articles reporting decision-analytic models provide enough information to enable decision makers in different jurisdictions to fully appreciate the variability of results according to location and be able to apply the evaluation to their own setting. The topics are: definition of target decision maker or jurisdiction, transparent reporting of model specification, relevance of data inputs to target decision maker or jurisdiction, and assessment of robustness of model to variation in data inputs within and between jurisdictions. It should be noted that most studies state the target decision maker or jurisdiction, but with less information provided on the other three topics [18].

## Steps to determine the transferability of studies

In Table 1 three steps are described that consider the availability of data and help to determine whether simple or more elabo-

> Even among countries with similar healthcare systems there are differences in the results of economic evaluations.

rate methods for adjusting results of economic evaluations to a particular jurisdiction are needed [2]. Firstly, an economic evaluation must meet three general knock-out criteria [4]. These criteria help to determine which studies can be transferred to the decision country. Both the experimental technology and the comparator(s) should be relevant in the jurisdiction of interest, otherwise the cost-effectiveness results are irrelevant. Furthermore, if the methodological quality of the study does not meet local standards, the transfer of the estimate is not valid. When the economic evaluation does not fulfil these three criteria, then the results are not transferable because the starting point of the evaluation is irrelevant [2, 4].




In the second step, the most important transferability factors [4] will be used to determine the level of correspondence between study country and decision country to decide if the economic evaluationis transferable. It is possible that only a simple adjustment procedure is necessary to transfer the economic evaluation results to the decision country. Therefore, the transferability factors should be verified to find out which adjustments may be necessary to be able to use the results. For instance, the setting where a patient is treated, e.g. hospital setting or family physician, can differ between countries. Therefore, practice variation between jurisdictions may make the transferability of the results of economic evaluations impossible without adjustment, for example, costs. Furthermore, differences in absolute and relative prices make recalculation necessary and therefore jurisdiction-specific price data might be required. In addition, the definition of the time horizon of the analysis can be a problem as the guidelines might differ between jurisdictions. Other characteristics of existing economic evaluations for which adjustment may be required, concern the perspective that is used, the discount rate applied and value sets used for the valuation of health states [2, 4, 15].

When it becomes clear that the available economic evaluation results are not directly transferable through simple adjustments the last step should be considered. Step three indicates that there are two remaining options. If the jurisdiction of interest has participated in a multinational clinical trial in which data on resource use and/or costs have been collected, then the preferred strategy would be to analyse the individual patient data. When the individual patient data are available there are some analytical approaches to calculate adjusted cost-effectiveness estimates for this jurisdiction. The analytic approaches address two sets of objectives. The first is to evaluate whether there is evidence of heterogeneity across jurisdictions included in the trial and to explore the potential sources of heterogeneity. The second objective is to obtain estimates of incremental resource use, cost and/or cost-effectiveness that are suitable for decision-making within particular jurisdictions that may or may not have been included. When economic evaluation was undertaken outside the jurisdiction of interest, a modelling approach would be required, using as much clinical and cost data as possible from the jurisdiction of interest. In general, the structure of a model will be determined by the clinical course of a disease and the effects of (a set of) interventions. Depending on the type of model selected, the structure embodies the choice of states/pathways and how they interact. However, there may be legitimate differences in model structure between jurisdictions and this is related to differences in the specified decision problem [2].

## Conclusion

The increasing pressure on healthcare decision makers to use scarce healthcare resources more efficiently has resulted in an enlarged demand for evidence from economic evaluations. Nevertheless, conducting an economic assessment of each intervention for each jurisdiction will result in inefficient use of evaluation resources. As a result, decision makers will increasingly be looking at the applicability of using economic evaluation results from abroad. However, there is sufficient evidence that economic evaluation results can vary across jurisdictions and that a number of factors may be a threat to the transferability of economic evalu-

ations. Thus, decision makers should be aware of the factors affecting the transferability of data from another jurisdiction. In our opinion, the most feasible option is to use the steps as proposed by the ISPOR task force [2].

## References


1. Magnell C, Brown L, Moskowitz A, et al. Chapter 6 Health care evaluation: issues in transferability. In: Project TOH, editor. Health technologies and decision making. Paris: OECD; 2005.
2. Drummond M, Barbieri M, Cook JR, et al. Transferability of economic evaluations across jurisdictions. ISPOR Good Research Practices Task Force Report. Value in Health 2009;12(4):409-18.
3. Späth HM, Carrère MO, Fervers B, et al. Analysis of the eligibility of published economic evaluations for transfer to a given health care system. Methodological approach and application to the French healthcare system. Health Policy. 1999;49(3):161-77.
4. Welte R, Feenstra F, Jager H, et al. A decision chart for assessing and improving the transferability of economic evaluation results between countries. Pharmacoeconomics. 2004;22(13):857-76.
5. Drummond MF, Pang F. Chapter 11 Transferability of economic evaluation results. In: Drummond MF, McGuire A, editors. Economic evaluation in health care. Merging theory with practice. Oxford: Oxford University Press; 2005.
6. Hutubessy R, Chrisholm D, Tan-Torres Edejer T, WHO-CHOICE. Generalized cost-effectiveness analysis for national-level priority-setting in the health sector. Cost Effectiveness and Resource Allocation. 2003;1(8).
7. Mason J. The generalisability of pharmacoeconomic studies. Pharmacoeconomics. 1997;11(6):503-14.
8. Willke RJ. Tailor-made or off-the-rack? The problem of transferability of health economic data. Expert Review of Pharmacoeconomics and Outcome Research. 2003; 3(1):1-4.
9. Mulligan J-A, Fox-Rushby J. Chapter 18 Transferring cost-effectiveness data across space and time. In: Fox-Rushby J, Cairns J, editors. Economic Evaluation: Open University Press; 2005.
10. Li S. How to improve pharmacoeconomic data generalisability between different countries. Expert Opin on Pharmacother. 2007;8(10):1409-13.
11. Barbieri M, Drummond MF, Wilke R, et al. Variability of cost-effectiveness estimates for pharmaceuticals in Western Europe: lessons for inferring generalizability. Value in Health. 2005;8(1):10-23.
12. Sculpher MJ, Pang FS, Manca A, et al. Generalisability in economic evaluation studies in healthcare: a review and case studies: NHS R&D HTA programme; 2004. Report No. 49.
13. Goeree R, Burke N, O'Reilly D, et al. Transferability of economic evaluations: approaches and factors to consider when using results from one geographic area for another. Cur Med Res Opin. 2007;23(4):671-82.
14. Oostenbrink JB, Koopmanschap MA, Rutten FFH. Standardisation of costs. The Dutch manual for costing in economic evaluations. Pharmacoeconomics. 2002;20(7): 443-54.
15. Szende A, Oppe M, Devlin N. EQ-5D value sets: inventory, comparative review and user guide. Dordrecht: Springer; 2007.
16. Knies S, Evers SMAA, Candel MJJM, Severens JL, Ament AJHA. Utilities of the EQ-5D. Transferable or not? Pharmacoeconomics 2009;27(9):767-79.
17. Boulenger S, Nixon J, Drummond MF, et al. Can economic evaluations be made more transferable? Eur J Health Econ. 2005;4(6): 334-46.
18. Urdahl H, Manca A, Sculpher M. Assessing generalisability in model-based economic evaluation studies. A Structured Review in Osteoporosis. Pharmacoeconomics. 2006;24(12):1181-97.