

HTAi

Background Paper

Transferability of HTA

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Introduction

HTA is a tool to support health systems to make decisions about allocating their limited health care resources. The recent growth of interest in extending universal health coverage (UHC) has increased interest in the use of HTA as a decision support tool.

In turn, HTA needs to be efficient and effective if investment in HTA is to be a sensible use of money. One important part of ensuring this will be to avoid duplication of effort by making the best possible use of existing information, and ensuring that when resources devoted to HTA are generating new information, it is likely to be of sufficient value to justify its cost.

This Briefing Paper will set out the issues to be addressed in considering when health systems can benefit from the transfer of HTA processes, decisions and/or data. Such issues include whether, or in what circumstances, countries can efficiently:

- copy institutional arrangements as to how HTA is organised or used in decision making;
- transfer decisions about the use of a particular technology;
- use some or all of a review of evidence, or a model or data about a technology;
- adapt a review of evidence or a model with the use of some local data;
- Collect or require local data and/ or conduct a local review of the evidence.

We discuss the different kinds of decisions that may or may not be transferred, the different degrees of transfer possible, and how decisions can be adapted to different contexts. We also discuss the practical and theoretical barriers to transferability.

Overall, we conclude that some of the barriers to transferability may be lower than is generally believed, and that transfer of HTA represents a real opportunity for making efficient decisions in an efficient manner, though the practical challenges should not be underestimated. This in turn raises questions as to whether:

- HTA bodies who are willing to see their reports and recommendations used by others could structure their content in a more accessible way;
- Regional collaboration is a vehicle for increasing transferability;
- Greater clarity could be given as to when (and why) local data will be required – whether commissioned by the public sector or required from the manufacturer.

It also raises issues for pharmaceutical companies undertaking global clinical development programmes pre- and post- launch for their drugs. These include:

- Having a clear understanding as to when (and why) one or more of pre-launch efficacy studies, "at launch" estimates of effectiveness or of cost-effectiveness using global health outcomes models, need to be supplemented or adapted with local studies or data, and whether or not they will be expected to provide the data;
- Understanding the likely acceptability of post-launch studies of product effectiveness in different settings.

The paper is structured as follows:

- It begins by distinguishing between different types of HTA
- It then looks at transferability issues relating to how HTA is organised
- It then looks at transferability issues relating to decisions and evidence relating to technologies and clinical guidelines

Types of HTA decisions

The first issue to consider is the type of decisions that we are discussing.

We can categorise HTA into three types¹:

1. HTA which is about assessing options for improving the efficiency of the organizational systems or architecture of the health care system. This includes how HTA is organised to support decision making.
2. HTA aimed at developing clinical practice guidelines or the way in which individual technologies are combined with and within a delivery system to manage patient clinical pathways efficiently
3. HTA aimed at appraisal of individual technologies, or groups of closely related technologies

As it makes more sense to begin at the system level, we consider, briefly, the potential transferability of aspects of the HTA system including the role of HTA and how it is organised.

Transferability of health system and HTA system characteristics

There is general recognition of the benefits of learning from the HTA experiences of others, by observing how health care in general, and HTA in particular, are carried out in similar countries: there may be willingness to consider the transferability of the kinds of activities involved in HTA, independently of expectations of the ability to transfer data, evidence reviews, models and decisions themselves.

Aspects of HTA *systems* that may or may not be transferable include:

- the scope of HTA – the types of technologies assessed;
- the referral process – who chooses what is reviewed by the HTA body?
- how the assessment of the evidence and the appraisal and decision making are organised (for example the involvement of external academic groups in the evidence assessment process);
- the role of the manufacturer – for example in making a submission or commenting on a review of evidence;
- any involvement of patients and patient groups in the process;
- the nature of any appeal process;
- the output of the process – a recommendation on price or on listing / access for some or all of the population groups that could benefit.

How HTA should or could be organised will in part depend on the structure of the health system – HTA is a tool to support decision making within the health system. It can be used at many different levels including:

- a national or system level, for example to decide which services are provided in a “basic package” of health coverage or to decide which drugs are listed for reimbursement under a pharmaceutical benefit package;
- a provincial or local level to supplement (or not) coverage provided at the national level;
- at a provider level to decide, given the constraints of budgets and provider reimbursement by the health system, which services are provided or what is included in a clinical guideline to manage patients in a particular disease area.

A series of publications have attempted to set out good practice for the conduct of HTA at the central, system, level. The most important series is by Drummond et al.² They set out a series of good practice principles – summarised in Table 1 below - and then explore how well they have been applied by HTA bodies

around the world. They reiterate with more detailed audit questions within each of the principles in a later paper.³

Table 1: Key principles for the improved conduct of health technology assessments (HTA) for resource allocation decisions

Principle 1:	The goal and scope of the HTA should be explicit and relevant to its use
Principle 2:	HTA should be an unbiased and transparent exercise
Principle 3:	HTA should include all relevant technologies
Principle 4:	A clear system for setting priorities for hta should exist
Principle 5:	HTA should incorporate appropriate methods for assessing costs and benefits
Principle 6:	HTAs should consider a wide range of evidence and outcomes
Principle 7:	A full societal perspective should be considered when undertaking htas
Principle 8:	HTAs should explicitly characterize uncertainty surrounding estimates
Principle 9:	HTAs should consider and address issues of generalizability and transferability examination of the generalizability and transferability
Principle 10:	Those conducting HTAs should actively engage all key stakeholder groups
Principle 11:	Those undertaking HTAs should actively seek all available data
Principle 12:	The implementation of HTA findings needs to be monitored
Principle 13:	HTA should be timely
Principle 14:	HTA findings need to be communicated appropriately to different decision makers
Principle 15:	The link between HTA findings and decision-making processes needs to be transparent and clearly defined

Source: Drummond et al. (2012)²

One exploration study has been undertaken recently by CRA⁴. However, the Drummond et al. approach has been criticised as being “context free”, i.e. not recognising that how HTA is used is not an absolute but relative to the decision making and cultural context. In particular, good practice use of HTA in a hospital setting – the typical budget constrained decision makers in many health systems – may not conform to the Drummond et al. principles⁵. Indeed, CRA⁴ set out key challenges that must be met if the underlying objective of improving health outcomes and related benefits is to be achieved:

- overcoming the difficulties of implementing decisions;
- understanding the real displacement when clinicians face budget constraints;
- specifying the counterfactual that the HTA body is being compared with.

That said, health systems may approach HTA organisation in different ways either because of real underlying differences of belief about what works, or simply as a result of how their systems happen to have evolved.

It is worth at this point spending a few moments on issues around the transfer of institutional arrangements more generally. Can health systems learn from each other about how to structure their health systems – the balance between primary and secondary care, say, or the role of fee-for-service, Diagnostic Resource Group, or capitation payments for providers – have potential for gains through transfer of best practices? The answer is yes, if (i) the evidence base is strong and (ii) the international studies are applicable to a different health system. Whilst the Drummond et al. principles for the operation of an HTA system are not evidence based, arguably they represent a starting point for thinking about aspects of process that may or may not be transferable.

Transferability of individual decisions, reviews of evidence, models and data

As outlined above, most HTA relates to decisions about guidelines and about individual health technologies (typically medicines, vaccines, and devices, but also surgical and other interventions), and the evidence reviews, modelling and data inputs which inform these decisions. These HTA assessments then inform decision making (appraisal) as to whether or not these technologies are to be made available or funded by the health system.

Transferability of HTA in this context is therefore concerned with the potential for profitable transfer of HTA decisions, evidence reviews, modelling and data inputs between jurisdictions. The potential for transferability of HTA at this level is likely to depend on:

- population characteristics including baseline risk for disease;
- existing patterns of use of technologies, both which technologies and how diseases are managed;
- the effectiveness with which the new technology will be used;
- in the case of a cost-effectiveness study, the resources used in the clinical path and the prices of those resources.

Generalizability and transferability

Note that if a decision is to be generalizable, this implies that both the underlying evidence and the decision criteria are generalizable, i.e. are relevant to the other health system. This is unlikely; decision criteria are likely to be country specific as they are highly dependent on factors such as the health care budget and social preferences.

Focusing on studies (such as an evidence review or a cost-effectiveness study using a decision analytical model) rather than a modelling or data inputs, to begin with, we distinguish between two standards by which we might judge whether a study in one health system can be used by another:

1. First we have "generalizability", which is the ability to directly apply studies from one health system in another. So a study generated in health system A is generalizable to health system B if B would arrive at exactly the same results as A were it to replicate the study in its own system. Clearly this is a very demanding standard for any two health systems to meet.
2. Second we have "transferability", which is the ability of studies to be adapted for use in at least one other country. Continuing our example from above, health system A's studies are "transferable" to health system B if it is possible for health system B to change some aspect of the analysis or data in the study— recalculate the incremental cost based on prices in its' health system, for example – in order to arrive at the study findings health system B would have found on its own, had it undertaken the study. Transferability is a much lower standard than generalizability, since it admits potentially significant differences between health systems, and permits relevant adjustments. Note that transferability requires that the differences between health systems are known and measurable, and that the original study is sufficiently transparent to make the relevant adjustments possible. In the above example, health system B would not have been able to adapt health system A's study based on differences in costs if it was not clear what role costs had played in the study analysis and conclusions for health system A.

Note that even if a study is neither generalizable nor transferable, it may still be possible to transfer some of the data used in the study. For example, imagine that the unit costs and patterns of clinical practice in health system B differ substantially from those in health system A, and therefore health system A's studies are not considered transferable. Yet, the estimated relative efficacy of a drug used as an input in health system A's HTA may be applicable to health system B if an indirect comparison can be made between the treatment currently used in health system A and that used in health system B. There would be benefit in using this data rather than generating it locally.

Note that, as with studies, data can be both generalizable, as in the example above, where health system A's relative efficacy data is directly relevant to health system B, or transferable, where the data is adjusted for the circumstances of a different health system. For example, differences in current practice could mean that the appropriate comparator differs between health system A and health system B, but health system A's data showing incremental health gain for the wrong comparator can be adjusted by extrapolating (using indirect comparisons) to the relevant figures for the comparator in health system B. Of course, there may be a concern as to whether similar relative *efficacy* will be reflected in similar relative *effectiveness*, which will depend on how the technologies are used in routine clinical practice.

Potential for transferability of HTA evidence, models and data

There are two ways in which we can consider the potential for transferability. The first is to look at what decision makers think. Evidence suggests that, unsurprisingly, decision makers consider some types of data to be more easily transferrable than others. Pichon-Riviere et al.⁶ (2012) conducted a survey in Latin America and the Caribbean, and found that of decision makers who reported using HTA reports to inform policy decisions, 75.7% used reports from other jurisdictions (52.6% of these used HTA reports from non-Latin American countries). Decision makers reported that:

- information regarding the description of the technology, safety, and efficacy or effectiveness were the most useful when using reports from other jurisdictions;
- information about ethical/legal/social aspects, budget impact, economic evaluation and organisational issues was considered less easily transferrable.

Similarly, a review of pharmacoeconomic guidelines used by HTA bodies⁷ found that:

- relative treatment effect was broadly considered to be highly transferrable;
- baseline risk and unit costs were consistently considered to be of low transferability;
- resource use and utility values were considered to be of low transferability in the majority of cases.

The second source of evidence is academic studies of criteria that may have to be met before a study in one health system could be transferable to another. A systematic review⁸ of the transferability literature aimed to identify factors which are perceived to influence the transferability of economic evaluations. A total of 102 conceptual and empirical papers were included in the review, and 77 separate factors were identified. These are sub-divided into five broad categories, which are shown in Table 2 alongside some examples.

Table 2: Factors affecting transferability of economic evaluations

Category	Examples
Patient characteristics	Demographics, education, socio-economic status, risk factors, medical history, lifestyle, mortality rates, culture.
Disease characteristics	Epidemiology, disease severity, case mix, disease interaction, co-morbidity, concurrent medications.
Provider characteristics	Clinical practice, conventions, guidelines, experience, training, skills, quality of care, method of remuneration.
Health care system characteristics	Absolute/relative prices, available resources, level of technological advancement, capacity utilization.
Methodological characteristics	Costing methodology, estimation procedures, study perspective, clinical outcome measures, discount rates.

Source: Goeree et al (2007)⁸

These factors perceived to influence transferability can be considered as potential barriers to the transfer of HTA. Identification of such barriers is valuable for developing tools and checklists which can be used to guide transfer of HTA across jurisdictions. There are several such tools available in the literature. A review of these is presented by Goeree et al (2011)⁹; seven studies meet their inclusion criteria, all of which are replicated and discussed in the review paper (see Appendix A for two examples of inclusion criteria).

Importantly, whilst identification of barriers is helpful for determining which elements of decisions and data can and cannot be reliably transferred, we need to be aware that the alternative is not costless perfect local data collection, modelling, analysis and evidence review. As there is uncertainty associated with the applicability of transferring studies, so there maybe uncertainty about the quality of any local replication. As such, we need to make decisions about transferability on the basis of the expected value of improved accuracy, set against the cost of replicating HTA analyses and the uncertainty as to the reliability of their results.

Potential for collaboration

Clearly, transfer of HTA will be easier between countries which are relatively good match for each other as measured by the metrics outlined above (populations characteristics, disease characteristics etc). Taking this further, where there are likely to be similarities between health systems, regional collaborations may well be an efficient approach to conducting HTA. EUnetHTA in Europe, HTAsiaLink in Asia and REDETSA in The Americas are examples of such collaborations.

The work of HTAsiaLink will be addressed in the Policy Forum meeting so we do not discuss further. In the case of REDETSA, the degree of heterogeneity between HTA systems has led to the sharing of approaches to establishing and running HTA systems, and related issues such as building up capacity. In contrast, the EUnetHTA collaboration has embarked explicitly on a programme of Joint Action designed to reduce duplication of effort in assessing the relative effectiveness of medicines. This has involved strands of work designed to achieve:

- A shared view (The HTA Core Model) of what is required in HTA submissions, including a Rapid Relative Effectiveness Review (REA) at the launch of a technology;
- A degree of consensus on the methods to be used to generate evidence;
- Pilot REA reviews of technologies in which two HTA bodies undertake a review on behalf of the whole group of HTA bodies.

The intent is that the EUnetHTA collaboration becomes self-sustaining, i.e. collaboration leads to the sharing of pan-European relative effectiveness assessments as an input to local decision making on pricing and reimbursement.

Local barriers to transferability of HTA decisions, data, models and evidence assessments

It is clear that transfer of data, models and evidence assessments, may provide real opportunities for health systems to reduce the costs and increase the efficiency of HTA decision making. However, in some cases transfer of elements of HTA could be seen as politically sensitive. Relying on the decisions or analysis (evidence assessments) of other health systems could be seen as involving some apparent sacrifice of national sovereignty.

These concerns are less likely to arise where reviews, data or models are transferred. Provided final authority as to the assessment of evidence is retained by domestic HTA bodies and decisions about priorities and reimbursement are made locally, the use of cost or efficacy information from elsewhere is less likely to be perceived negatively, provided that the information meets the relevance criteria outlined above.

It is not simply, however, a question of applicability. For many health systems the process by which a decision is made may have some inherent value, distinct from the value of the decision itself. If a health system, or its polity, believes that process matters then the framework above will not capture all the benefits of replicating existing HTA domestically. Conversely, HTA bodies and decision makers with robust deliberative decision processes may be more willing to use studies and data from elsewhere, because they will be explicit as to how it is used in the assessment and decision making processes.

Drawing these points together, health systems are more likely to be receptive to use of information from elsewhere where these approaches do not directly determine the final allocation of health care.

How to increase the potential for HTA transferability

Having established that HTA transfer can represent a valuable resource saving for the HTA systems of recipient health systems, we will now consider how HTA producing health systems can tailor their decisions to maximise opportunities for transfer. Note that the value of ensuring that studies are transferable has

the potential to be large and widespread, and the benefit to the producing health system will grow as more health systems follow suit, forming collaborations, and allowing the full value of HTA research to be realised.

The first key point is that, in order to be transferable, studies should be as transparent as possible, so that it is possible for recipient health systems to see which inputs actually matter most, and how sensitive results are to changes in parameter values. Reporting could be in "baskets" of dimensions with, for example, more uniform reporting of evidence and conclusions in the baskets of clinical effectiveness, economic considerations, and "other dimensions" (such as wider social benefits, burden of illness, and ethical considerations). Economic considerations can mean different things in different systems, according to the "HTA archetype". Budget impact, including net of cost-offsets that can be reasonably expected to occur, is one meaning, cost-effectiveness is another. Ideally, readers from other health systems should be able to quickly determine whether the study findings in question are sensitive to plausible differences in, say, the cost of existing treatments, or health gain valuation. If a study can be disaggregated into its constituent elements, and the analysis and data underlying each element are freely available, then each part of the HTA process can potentially benefit other nations' systems.

The same general argument applies to decisions about health system design, including the design of the HTA process. Since transferability means that information can be valuable outside the health system which produces it, more information, made freely and easily available, leads to greater potential gains.

Health systems which find themselves producing HTA on which other health systems might seek to rely can increase the global value of their work by making it freely available, transparent and by providing the inputs into the study in a disaggregated, modular format, so that other health systems can pick and choose only the parts of the decision which are in fact transferable.

The question in relation to barriers to transferability built in to the HTA system is not whether they exist, but whether the expected size of the errors they induce is sufficiently large to make it worthwhile for health systems to expend resources replicating locally existing studies. A difficult balance has to be struck between the risk of transferring evidence and data that may not be locally applicable and seeking to do too much locally which overburdens the HTA system. Note that the cost of an overburdened HTA system goes beyond additional government expenditure. A health system which tries to conduct more HTA than its resources permit may also impose delay on technology approval, leading to burdens imposed on patients, who are denied timely access to new technologies, and producers, whose incentive to innovate is reduced.

Conclusions

Health systems need not always reinvent the wheel when faced with the task of assessing a health technology, whether that "technology" is as small as an individual medicine or as big as a way of structuring the system as a whole.

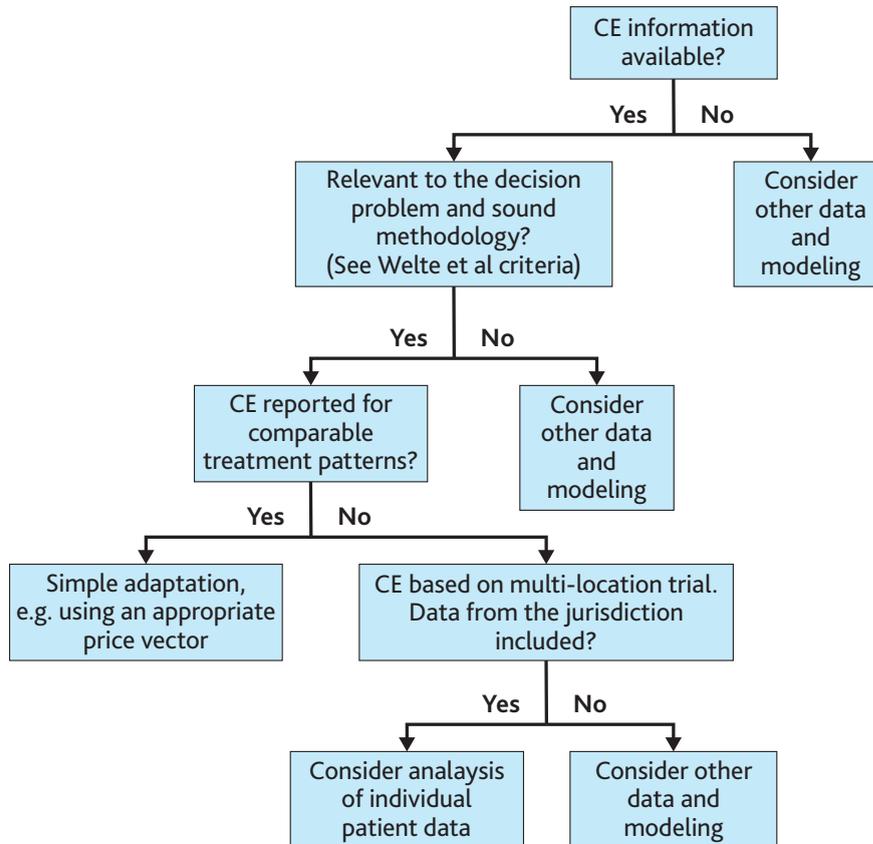
They can benefit from considering what other health systems have done in similar circumstances, and should think carefully about the relative costs and benefits of replicating another HTA process or transferring an existing decision. However, a number of difficult issues arise which may limit the theoretical benefits and increase the practical difficulties of achieving them.

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Appendix A: Examples of Approaches

Drummond et al., (2009)¹⁰ application algorithm



Welte et al. (2004)¹¹ criteria

General and specific knock out criteria are provided:

- **General knock-out criteria:** Welte et al. claim that if any of the following criteria apply then transfer of HTA between countries is almost impossible:
 - The evaluated technology is not comparable to the one that shall be used in the decision country
 - The comparator is not comparable to the one that is relevant to the decision country. An example is a comparator drug that is not licensed in the decision country
 - The study does not possess an acceptable quality, i.e. it does not live up to the standards required in the decision context, e.g. there is double counting of costs.
- **Specific knock-out criteria:** all transferability factors (such as those listed in Table 1) are considered potential knock out criteria if they are not applicable to the recipient country or if they cannot be assessed properly.



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