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The role of HTA in coverage and pricing decisions: A cross-country comparison

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Since the late 1970s, many European countries have established health technology assessment (HTA) systems to inform coverage and pricing decisions. These countries use HTA to systematically determine the relative 'value for money' provided by new technologies and to give providers and patients information to make treatment choices. This, in turn, serves to encourage the efficient and effective use of health technologies and to support innovation by identifying and rewarding high-value products.

This overview article explores the use of HTA in coverage and pricing decisions, with a focus on pharmaceuticals, in six European countries with established HTA systems – Denmark, England, France, Germany, the Netherlands and Sweden.

HTA functions and governance

Coverage decisions based on HTA typically involve two stages: an *assessment* of a drug's relative costs and benefits, followed by an *appraisal* (interpretation and consideration) of the evidence to inform coverage decisions. Each of the six countries has advisory or regulatory HTA bodies, sometimes referred to as drug review bodies, involved in coverage decision making (and sometimes pricing) (Table 1). Both advisory and regulatory bodies conduct or coordinate assessments, but only regulatory bodies have the remit to make *decisions* about coverage and/or pricing based on the review. Advisory bodies, alternatively, make coverage and/or pricing *recommendations* to government authorities, who then render the final coverage and/or pricing determination. In countries with advisory bodies (France, Germany, the Netherlands), the Ministry of Health oversees the assessment process to some degree.[1]

External organizations are sometimes involved in assessments. England's National Institute for Health and Clinical Excellence (NICE), for example, coordinates independent reviews by academic research centres. Moreover, almost all countries have dedicated national HTA agencies that coordinate and disseminate assessment reports on health technologies and other interventions.[2] However, they are typically not involved in making coverage and pricing decisions.

Stakeholder involvement

The decisions resulting from HTA can have a significant impact on treatment availability as well as clinical practice. Consequently, a range of stakeholders, including policy makers, providers, industry, and patients, are interested in the process and want to ensure that their views are considered.

Patients and consumer groups are the least likely stakeholders to be involved in the assessment process. Increasingly, however, several review bodies (in England, Germany and Sweden) recognize the importance of involving patients and consumers, as they can provide useful insight into a drug's 'real world' value. For example, NICE in England has established a Citizens Council to gather public perspectives on key social and ethical issues, such as whether age and disease

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Table 1: Key drug review and decision making bodies in select countries, 2008

Country	Review process		Decision-making process	
	Review Body - Role	Function	Pricing	Coverage
Denmark	Reimbursement Committee of the Danish Medicines Agency (DKMA) – Regulatory	Coverage	DKMA[a]	DKMA
England	National Institute for Health and Clinical Excellence (NICE) – Regulatory	Coverage	Department of Health[a]	NICE/Department of Health
France	National Health Authority, Transparency Commission (TC) – Advisory	Coverage	CEPS	Ministry of Health, Social Affairs, and Social Insurance
	National Health Authority, Economic Committee for Health Products (CEPS) – Regulatory	Pricing		
Germany	Institute for Quality and Efficiency in Health Care (IQWiG) – Advisory	Coverage and pricing	Federal Association of Sickness Funds[a]	Ministry of Health/ Federal Joint Committee
Netherlands	Health Care Insurance Board, Committee for Pharmaceutical Aid (CHF) – Advisory	Coverage and pricing	Ministry of Health, Welfare, and Sport	Ministry of Health, Welfare, and Sport
Sweden	Dental and Pharmaceutical Benefits Agency (TLV) – Regulatory[b]	Coverage and pricing	LFN	LFN

[a] Decision-making influence is limited due to the use of free pricing, where prices are set by the manufacturer.
[b] The TLV was previously named the Pharmaceutical Benefits Board (LFN).

severity should be taken into account in NICE reviews.

In all of the six countries, manufacturers are generally involved prior to the assessment process, when they submit a dossier of evidence* to the review body. They are not usually engaged in the actual assessment or appraisal process. Involving industry throughout the HTA process may be beneficial, given its role in producing and interpreting much of the clinical data employed in assessments; however, it can be controversial, giving rise to fears that industry may reduce the objectivity of assessments.

Although stakeholder involvement is generally resource intensive and may introduce other challenges, such as extending the time required to complete assessments, it can enhance the relevance of and trust in the HTA process.

Conducting assessments

Assessments involve many of the same principles and processes across the six countries, but they often differ in key areas, such as selecting which drugs to review, the type and quality of evidence required, and methodological approaches. Table 2 shows the various national approaches to conducting assessments. Many countries publish guidelines outlining their evidence and methodological requirements, but these often vary in detail and transparency.**

It typically takes six months to two years to review pharmaceuticals for coverage, which is often seen as a barrier to timely patient access to new products. France and the Netherlands have introduced expedited review processes for highly-innovative drugs or for those treating life-threatening illnesses. England has led efforts to shorten reviews by introducing fast-track processes such as Single Technology Appraisals (STAs) (see UK case study). These place more emphasis on manufacturer data and less on extensive external systematic review and consultation, which allows drugs to be available a few months after launch.

Decision making and implementation

Applying HTA to coverage decisions

Following appraisal of the evidence, review bodies employ a variety of criteria to inform coverage decisions. In each of the selected countries, a drug's relative therapeutic benefit is the most important criterion in determining coverage status, followed by cost-effectiveness (measured using cost per quality-adjusted life year (QALY) ratios.[3] Cost-effectiveness is particularly important for drugs that are expensive and/or widely used, have new indications, or whose benefits differ by indication or patient sub-group. England, Germany, the Netherlands and Sweden outline more explicitly the use of cost-effectiveness in decision making, whereas its role in the review process is limited or not always clear in Denmark and France. The situation in France may be changing, however (see France case study).

Some countries use a cost-effectiveness or price threshold to establish whether a drug provides value for money and to determine coverage status. A threshold generally represents the amount of money a society is willing to pay for an additional unit of health outcome (i.e., an additional QALY). Such 'decision rules' are often implicit and case-dependent. The value of the threshold varies by country, ranging from a maximum of €20,000 in the Netherlands to €45,000 in Sweden.[4,5] The Netherlands and Sweden are considering adopting a revised approach that adjusts the threshold according to need (disease severity) or equity considerations (see the Netherlands case study). Instead of employing a cost per QALY threshold, Germany has recently proposed the use of an efficiency frontier (see Germany case study).

* A dossier typically includes all available data and evidence regarding a pharmaceutical (approved indications, clinical benefit and, sometimes, cost-effectiveness).

** For country guidelines see: Pharmacoeconomic guidelines around the world. International Society for Pharmacoeconomics and Outcomes Research website, 2004. Available at: http://www.ispor.org/PEguidelines/index.asp

Table 2: Comparative pharmaceutical review methods used in select countries, 2008

	Denmark	England	France	Germany	Netherlands	Sweden
Selection criteria for drugs to review	Every new drug[a]	Department of Health refers drugs to be prioritized based on criteria, such as health impact, disease burden, and clinical/policy relevance	Every new drug[a]	Drugs that cannot be classified under reference pricing system	Drugs that cannot be classified under reference pricing system	Every new drug[a]
Evidence requirements	RCT data preferred; health economic information recommended, but not required Source: Evidence from manufacturer dossier	RCT data preferred; health economic information required Source: Systematic reviews and analyses of clinical and economic studies; may or may not include manufacturer data	RCT data preferred; health economic information recommended, but not required Source: Evidence from manufacturer dossier	RCT data preferred; health economic information required Source: Systematic reviews and analyses of clinical and economic studies; may or may not include manufacturer data	RCT data preferred; health economic information required Source: Evidence from manufacturer dossier	RCT data preferred; health economic information required Source: Systematic reviews and analyses of clinical and economic studies; may or may not include manufacturer data
Preferred or required approach (health economic component)	N/A	• CEA • CUA	• CEA • CUA • CMA	• Efficiency frontier analysis	• CEA • CUA	•CEA •CMA
Choice of comparator	N/A	Current best alternative or routine treatment	Three comparators required from same therapeutic group: • most frequently used • cheapest • most recently added to positive list	Most effective treatment, most widely used, or routine treatment	Routine treatment	Three comparators required from same therapeutic group: • routine treatment • non-medical intervention • no treatment
Principal outcome measures	N/A	• Mortality • Morbidity • Quality of life	• Mortality • Morbidity • Quality of life	• Mortality • Morbidity • Quality of life	• Mortality • Morbidity • Quality of life	• Mortality • Morbidity • Quality of life • Willingness to pay
Costs	N/A	• Direct costs • Indirect costs, depending upon the assessment	• Varies by assessment	• Direct costs • Indirect costs	• Direct costs • Indirect costs not required, but if included must be reported separately	• Direct costs • Indirect costs

[a] This entails reviewing every new drug dossier submitted by manufacturers to support a coverage decision. Thus, in principal, manufacturers ultimately decide which drugs are reviewed.

Notes: N/A = not available; RCT = randomized controlled trial; CEA = cost-effectiveness analysis; CUA = cost-utility analysis; CMA = cost-minimization analysis.

Other decision criteria used by countries include availability of treatment alternatives as well as public health and budget impact. Many stakeholders contend that more consideration should be given to these factors and that greater transparency and explicitness is needed regarding how they factor into the decision process.

It is rare for a drug not be accepted for any level of coverage; rather, most are approved with conditions (for example, use only in certain indications or patient groups). Some countries have recently started to use conditional approvals in innovative ways to alleviate some of the uncertainty normally associated with pre-market review, especially for new or highly-innovative products. England, France, the Netherlands and Sweden have introduced risk-sharing agreements and/or coverage with evidence development (CED). These strategies link coverage to conditions such as meeting agreed cost, volume, market share and cost-effectiveness targets and/or the collection of post-market evidence and (re)evaluation. If the conditions are not met, then coverage may be withdrawn and/or the price reduced. For example, after NICE (controversially) recommended against the use of various products for multiple sclerosis, the government established a risk-sharing scheme with manufacturers to supply these treatments on the National Health Service (NHS). Under the scheme, patients were monitored annually and the amount paid for the treatments was adjusted on a sliding scale if patient outcomes differed from agreed cost-effectiveness targets.

HTA evidence can also be used to support pricing decisions, in what is termed 'value-based pricing' (VBP). Sweden introduced VBP in 2002; coverage and pricing decisions are based on an assessment of health needs and cost-effectiveness. For example, if the drug price requested by a manufacturer is unreasonably expensive in relation to the benefits or value provided, the drug would either not be covered or its price would be reduced. This approach has been heralded as a mechanism to obtain greater value for money and create a stronger link between coverage and pricing decisions. VBP is also being considered in England.[6]

While the assessment and appraisal process typically occurs prior to launch, some countries, namely the Netherlands and Sweden, also undertake systematic re-evaluation after a drug has been used in practice to identify products that do not demonstrate good value for money or become obsolete. Evidence from ex-post review is then used to determine areas for disinvestment (de-listing) or to modify pricing and coverage status, where appropriate. Denmark has recently announced a five-year review of the pricing and coverage status of existing pharmaceuticals,[7] and Sweden has been evaluating all drugs approved prior to 2002. England has also called for greater NICE involvement in supporting disinvestment.[8]

Implementing coverage decisions

In most of the six countries, national coverage decisions apply nationally, but in some countries, particularly Denmark, England and Sweden, regional and/or local authorities have some discretion in implementing national decisions. Consequently, local coverage arrangements may differ from national guidelines at the margin. Such variations can be attributed to a lack of additional funding and guidance to implement national coverage decisions, delayed local uptake of guidance, poor financial planning by local authorities, insufficient health economics expertise among local formulary committees, and divergent local health needs.

Successful implementation of coverage decisions is a key challenge for health systems. Review bodies use different strategies to enhance the implementation of pharmaceutical coverage decisions and/or recommendations, including information dissemination strategies (newsletters) to apprise stakeholders of recent decisions and policy changes (England); collaboration with various experts to promote implementation at the local level (Sweden); providing additional financial support to cover the cost of supplying new pharmaceuticals (Denmark, England, Sweden); and participation in international HTA networks (for example, the European Network for HTA) to facilitate methods development and enhance the transferability and transparency of HTA (England, France, Germany, Netherlands). Regulatory levers have also been used in Denmark and England to make decisions or guidance legally binding.

Conclusions

HTA has assumed an increasing role in pharmaceutical coverage decisions in Europe. Not only does it contribute to evidence-based decision making, it also assists in identifying products that offer the most value for money. The six countries reviewed here adopt different approaches to using HTA in coverage decisions, but all strive to ensure rigorous, relevant, and transparent assessments. Countries increasingly recognize that HTA is only useful if the process is timely, the resulting recommendations are used by policy makers, and decisions are implemented. Consequently, many countries have introduced innovative solutions to address these issues, such as risk-sharing agreements, expedited reviews, and greater stakeholder involvement. Other strategies gaining traction include greater use of HTA reviews for other health technologies and interventions (for example, medical devices, public health programmes) and in other sectors (see the Netherlands case study).

The use of HTA in pharmaceutical coverage decisions has grown substantially since the late 1990s and is likely to expand further, as national policy makers continue to face cost pressures and attempt to use evidence-based approaches to ensure the effectiveness, efficiency, and sustainability of their health systems. Consequently, more attention and resources are needed to improve strategies to enhance the drug review and policy process and to support the use of HTA in policy making.

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HTA in coverage and reimbursement decisions in France: toward a new paradigm?

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Role of HTA in coverage and pricing decisions

Benefits that are covered by the French national statutory health insurance (SHI) are defined in explicit positive lists. Medical goods or procedures are added to the positive list by either the Ministry of Health (MoH), in the case of pharmaceuticals and medical devices, or the SHI, in the case of procedures, based on the recommendation of devoted consultative committees of the National Health Authority (HAS). These committees are comprised of scientific experts, representatives of the MoH, SHI, and, when concerned, representatives of the industry. The recommendation of the committee(s) is also given to support price determinations.

HTA plays a central role in forming HAS's recommendation. To derive a coverage determination, HAS reviews evidence on the medical benefit of the technology or intervention, reflecting its clinical efficacy and the severity of the disease it is indicated to treat. In the case of drugs, the degree of medical benefit or therapeutic value is represented by a SMR (*Service medical rendu*) level. The HAS Transparency Committee also assesses the relative medical benefit of the technology in comparison to similar available treatments (termed the ASMR, *amelioration du service medical rendu*).[1]

Decisions on coverage depend on the level of SMR, which can range from insufficient to considerable (Table 1).

Information on the ASMR, denoting the level of therapeutic improvement, is used in subsequent price-setting. Drugs with major or important improvements and no competitors on the market are priced by the pharmaceutical companies themselves, but are reviewed by the HAS pricing committee (Economic Committee for Health Products, CEPS) to ensure that prices are consistent with those of main European markets. CEPS can also consider the drug's impact on public health. Drugs with moderate improvement are likely to be priced slightly above the nearest competitor (around 15%) and those with no improvement are priced below the price of any competitors already on the market. Most drugs assessed in 2007 were categorized as having an SMR of 'important', but an ASMR of 'no therapeutic improvement'.[2]

However, other criteria, in addition to the results of HTA, are taken into account in price-setting. In particular, consideration is given to projected sales levels, which depend on population need, recommended daily dosage, or the daily cost of treatment. This information is used to establish price-volume agreements between HAS and manufacturers.

Table 1: Rate of coverage of medicines by level of SMR

SMR (therapeutic value)	Serious disease (rate of coverage %)	Disease 'not usually of a serious nature' (rate of coverage %)
Major or considerable	65	35
Moderate or low	35	35
Insufficient	0	0

If agreed volume levels are exceeded, the price is lowered or companies are required to provide rebates to the SHI. A product's SMR and ASMR is reviewed once every five years.

Movement toward considerations of value for money

As discussed, coverage and pricing decisions in France are principally based upon clinical efficacy, not on cost-effectiveness or value to society. By not taking into account cost-effectiveness or 'value for money', it does not allow for prioritising public expenditure across different health technologies. As highlighted in the Overview article, this situation differs from other European countries.

However, the situation may be changing. In 2008, the Social Security Finance Act introduced the use of economic evaluation in HAS's review and recommendation. While this is considered a step forward, its use and implementation in practice is uncertain and currently under discussion. A HAS Commission for Economic Evaluation and Public Health (*Commission évaluation économique et de santé publique*, CEESP) was established in July 2008 to oversee the integration of cost-effectiveness into public decision making as well as clinical practice. As currently envisioned, in the first instance CCESP will issue a recommendation on a drug's cost-effectiveness, which will be considered alongside the advice of the Transparency Commission. HAS is also currently developing a societal benefit measure, SERC (*service rendu à la collectivité*), to capture not only the medical and economic costs and benefits of health services, but also important ethical, social, and legal considerations.[3] The SERC would more closely resemble

a 'full HTA'. While its use to date has been limited to screening programmes, there are plans to apply it to other interventions, such as pharmaceuticals.

Despite movement toward this new paradigm, there are several outstanding challenges to its development. First, there is mixed support for formal integration of economic evaluation in drug reviews. While it will be considered, a certain level of cost-effectiveness will not imply a defined coverage decision as in the case of SMR and ASMR. Second, drug prices in France are currently comparable to the European average and are often lower. Third, the French system is favourable to the uptake of innovative products, so a focus on cost-effectiveness may hinder innovation.

Considering these concerns, it is unlikely (at least in the short-run) that economic evaluation will directly influence coverage decisions. Rather, cost-effectiveness, or considerations of value for money, will be used to enlighten decision makers and clinicians on the broader benefits of a given treatment.

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HTA in Germany: The new 'frontier' of IQWiG methods

Thomas Mittendorf

HTA has been around in Germany for many years. In one of the first initiatives, the Ministry of Health commissioned HTA reports in the mid-1990s on a range of topics, including specific pharmaceuticals, procedures and health care services. This project was later formally transferred to the German Agency for Health Technology Assessment at the German Institute of Medical Documentation and Information (DIMDI), a division of the Ministry of Health. To date, the Agency has produced more than 100 reports. However, throughout the early 2000s, these reports had minimal impact, as decision makers in Germany had no legal obligation to consider health economic information in reimbursement decisions. Germany was and still is a market with free pricing, where there is no 'fourth hurdle' following market approval. That is, once a product receives market approval for use, it is reimbursed within the Statutory Health Insurance (SHI) system without having to demonstrate cost-effectiveness.

IQWiG assessments

In 2004, the introduction of the Institute for Quality and Efficiency in Health Care (IQWiG) dramatically changed the landscape. Its task at that time, among others, was to conduct assessments for the Federal Joint Committee (GBA), who has authority over reimbursement determinations. While HTA assumed a more influential role in GBA decisions following the inception of IQWiG, assessments continued to focus solely on available clinical evidence (principally from randomized controlled trials or RCTs), not cost-effectiveness. Two years ago the law was amended to broaden assessments to include cost-benefit assessments (CBA). Following the new mandate, IQWiG recently revised its methods to include a two-step process.[1] Firstly, the clinical evidence is assessed. If a product demonstrates a relative benefit over existing alternative treatments, it will then undergo CBA. However, only evidence from the first stage (clinical benefit) assessment is presumably allowed to be included. Moreover, departing from international standards, the CBA would entail the use of an 'efficiency frontier', as opposed to quality-adjusted life years (QALYs) to assess health benefit. While QALYs allow comparisons of costs and benefits across therapeutic areas, the efficiency frontier focuses on the relative value of different drugs within a given therapeutic area.

This raises several challenges as the benefit assessment typically only includes clinical RCT data, resulting in the exclusion of effectiveness data, which is generally an important input for CBAs. Furthermore, if an important and relevant patient-related outcome, such as quality of life, was not included in the RCTs under review, it will not be included in the CBA

Changing methods and remaining questions

At present, Germany is still in the phase of extensive discussions around the final methods that will be used by IQWiG moving forward. Some initial CBAs are currently being carried out by various research groups commissioned directly by IQWiG, and the scientific community is keenly awaiting the third pre-final version of the methods. After completion of these preliminary analyses and another round of expert hearings, CBAs will likely be formally integrated into the IQWiG process at the beginning of 2010.

In the interim, many questions remain surrounding IQWiG's proposed methods. Hotly debated issues encompass the following:

- What analysis perspective should be employed (payer or society);
- Whether CBA will entail all relevant benefit parameters, as opposed to only those gathered and considered in the clinical benefit assessment;
- Whether economic models will be used;
- Whether IQWiG should use a two-step process (clinical benefit assessment, then CBA) or if a full HTA approach is optimal, where clinical and economic benefits and costs are assessed in tandem;
- If the efficiency frontier concept is feasible.

The recent change in IQWiG's mandate has sparked significant national and international controversy in the past two years particularly with regard to the methods that it will employ in assessing the relative costs and benefits of new treatments.[2] Whatever will result from these discussions, and regardless of the results of major Federal elections at the end of this year in Germany, it is certain that some type of technology assessment will be required following market approval from now on. This may provide an avenue for payers to engage in direct price negotiations with the industry.

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The use and impact of HTA in decision making in the Netherlands

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In the Netherlands, HTA has evolved from a primarily academic research activity into policy research for improving health care on the national level.[1] This article briefly reviews some of the key issues surrounding the use of HTA in the Netherlands. Particular focus is given to the area of medical specialist care, where recent developments have led to more systematic use of HTA.

The use of HTA in different sectors

In the Netherlands, the use of HTA has been especially pronounced in the area of out-patient pharmaceuticals. In order for an innovative drug to get on the positive list with a premium price, a pharmaco-economic dossier has been obligatory since 2005. In other areas, the use of HTA has lagged behind.[2] For example, in the in-patient sector doctors freely took up new (sometime expensive) technologies, within the limits of the hospital budget. With their increased use, these technologies were gradually considered usual care and, as such, would become a legal entitlement for patients as part of the benefits package, without any formal evaluation. In other areas, such as those of long-term care and assistive devices, the use of HTA was even less common. This may, in part, reflect challenges in applying economic evaluation methods to different care sectors.

Currently, there is movement towards more systematic use of HTA in all health care sectors. For example, a programme examining the real-world cost-effectiveness of expensive in-patient drugs was initiated. Furthermore, HTA has been integrated into the application requirements for innovative interventions in the field of medical specialist care, as will be highlighted in the remainder of this article.

Medical specialist care and HTA: Evaluating DBCs

As part of reforms to create a more demand-driven, regulated hospital market, a hospital financing system based on 'diagnosis treatment combinations' (DBCs) was launched in 2005. The DBC financing system includes a description of all medical specialist care products and their prices. Consequently, new forms of care have to be translated into new DBCs. Unlike in the past, this allows an explicit consideration of the desirability of including new forms of care in the benefits package.

The HTA-based decision-making system can be summarized as follows.* When a new procedure is introduced into medical specialist care, a new DBC must be obtained from the DBC Maintenance Organization, an independent body whose board is comprised of members from hospital, insurer and patient associations. The applicant is asked to provide descriptions of the proposed DBC and the indications for treatment, as well as information on safety, cost-effectiveness and stakeholders' views. The Health Care Insurance Board (CVZ) then assesses

* More details about the HTA system can be found elsewhere.[3]

whether the new product meets evidence-based standards or is considered reasonable and adequate care, which comes down to a broad assessment of effectiveness. If this is indeed the case, an assessment will follow in which CVZ considers the product's necessity, in terms of disease severity and medical need; cost-effectiveness; and feasibility (budget impact and possible substitution to other, more expensive types of care). This results in a recommendation to the Minister of Health, Welfare, and Sports regarding whether the DBC should be included in the benefits package. The Minister, who has final decision-making authority regarding the benefits package, generally follows this advice, but may also consider the DBC's public health relevance (for example, affordability, necessity of care, etc.).

Given its recent introduction, we can only draw some tentative conclusions regarding the impact of HTA. The HTA principles reflect the belief that a service should only be added to the benefits package if there is strong evidence about its safety, effectiveness, and cost-effectiveness. However, especially in the area of medical specialist care, evidence is often incomplete and inconclusive in practice. This may explain why there is no requirement for applicants to produce evidence on the DBC that meets stringent standards. For example, an estimate of the costs per QALY is not mandatory. If the Minister truly adhered to the belief that a service should only be reimbursed if there is high-quality evidence, lack of information would by definition lead to a negative reimbursement decision. A more likely scenario is that decision makers will either reduce their reliance on data generated by research (relying on experts' opinions instead) or postpone the final decision by granting temporary reimbursement conditional upon collection of additional evidence. These courses of action have been practiced in other sectors of Dutch health care, and are expected to be pursued in the future.

Generally, in the coming years the focus should be on optimising transparency and consistency, such as when to decide to grant a temporary reimbursement status and ensuring that stakeholders from various backgrounds have the opportunity to be involved in the process. This will ensure greater acceptance of reimbursement decisions.

Cost-effectiveness threshold

Another noteworthy issue is that neither CVZ nor the Minister applies an explicit cost-effectiveness threshold in the decision-making process. Instead, cost-effectiveness is appraised in relation to other factors that enter into decisions, such as equity, the availability of other treatments, and budget impact.

Recently, the Dutch Council for Public Health and Health Care (RVZ) put forward the idea – which had been promoted earlier[4] – of varying the cost-effectiveness threshold with the severity of a condition.[5] The cost per QALY may be higher for very severe conditions (a tentative maximum of €80,000) than for mild conditions (a threshold of €20,000 or less). In other words, chances of funding increase when the cost-effectiveness ratio becomes more favourable, and/or when conditions get more severe. This RVZ report has attracted much public debate, but seems to reflect widely shared values. However, the Minister has announced that he will not treat the €80,000 threshold as an absolute limit.[6]

Conclusions

HTA is increasingly important in the Netherlands. The necessity, effectiveness and cost-effectiveness of diverse interventions are more systematically considered in delineating the benefits package. However, numerous challenges remain, such as the absence of a clear threshold value for cost-effectiveness and the relative lack of information in areas other than pharmaceutical care. The role of HTA will continue to be to support decisions, not to prescribe them. Still, the expansion of HTA throughout the health care sector, like in medical specialist care, should bring us closer to the ultimate aim of HTA, which is to improve the health of the population and promote efficient use of resources.

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More haste, less speed? The emerging practice of HTA in the United Kingdom

Michael Drummond

HTA has a long history in the United Kingdom (UK). The major shift in the conduct of HTA came in 1991, with the establishment of the NHS Research and Development Programme. Although the greatest expenditure was on primary research, HTA became an increasingly influential part of the programme. The National Coordinating Centre for Health Technology Assessment (NCCHTA) was later established in 1996 to handle the process of prioritising topics, commissioning studies, assessing the results from studies and disseminating the results.

However, much of the recent discussion on HTA in the UK has concerned the National Institute for Health and Clinical Excellence (NICE).[1] In some ways, the interest in NICE is surprising. NICE is not the only HTA entity in the UK, the Scottish Medicines Consortium (SMC) and the All Wales Medicines Strategy Group (AWMSG) being others, nor is it the first such entity in Europe. Bodies assessing the evidence on the clinical and cost-effectiveness of health technologies (especially drugs) have existed for several years in other European countries.

The NICE approach

The extensive discussions of NICE probably relate to the fact that it developed detailed and transparent procedures for the scoping of its technology appraisals and incorporated extensive stakeholder involvement. In addition, its assessments have typically been very rigorous, incorporating both a systematic review of the clinical literature and an economic model.[2] Also, these assessments are published in full by the NCCHTA.

NICE's distinctive approach to conducting technology appraisals, now called Multiple Technology Appraisals (MTAs), has led to several methodological advances, most notably in two areas: (i) mixed treatment comparisons,[3] where advanced statistical approaches are used to synthesize the clinical data in situations where head-to-head trials do not exist, and (ii) probabilistic sensitivity analysis, where the overall uncertainty surrounding estimates of cost-effectiveness is presented to decision makers.[4]

The other distinct feature of NICE's approach is the use of an explicit cost-effectiveness threshold. Following speculation on whether NICE had a view on what the NHS should be willing to pay for health technologies, Rawlins and Culyer[5] argued that technologies with an incremental cost per unit of health gain (i.e., a quality-adjusted life-year or QALY) of below £20,000 (about €22,000) were highly likely to be recommended, whereas those with a cost in excess of £30,000 (about €33,000) per QALY gained were unlikely to be recommended.

A move towards STAs

Times are changing; following widespread criticism over the time taken for NICE to undertake its assessments,[6] NICE is now conducting increasingly more single technology appraisals (STAs). These appraisals consider only a single technology in a single indication and involve a review of evidence submitted by the technology's manufacturer, rather than a de novo analysis. In addition, the provisional guidance is only sent to stakeholders for comment if it restricts the use of the technology within its licensed indications. NICE's STA approach mirrors those operating in most of the European countries, including the SMC.

Apart from being quicker, the STA approach is less resource-intensive, thus enabling more appraisals to be conducted within the available budget. However, some problems have arisen. First, as the STA approach places the burden of proof on the manufacturer, it is unclear what should be done in situations where the manufacturer is unable, or unwilling, to submit evidence.[7] Should the recommendation regarding the technology be negative (as in Scotland), or should NICE try to generate the evidence itself? Secondly, is there a risk that assessments are less rigorous, thereby increasing the uncertainty experienced by decision makers?

The impact of STAs

In a review of decisions on new cancer drugs, Mason and Drummond[8] detected a trend towards more negative decisions following the introduction of STAs, although there appeared to be multiple reasons for this. Finally, with NICE's extensive involvement of stakeholders, does more haste mean less speed? Haycox[9] points out that many of the delays in NICE technology appraisals occur after the first Appraisal Committee meeting, as a result of stakeholder comments and appeals.

The other distinctive feature of NICE's MTAs was that these often contained a review of a wide range of competing treatments for the condition concerned. Unlike drug (or technology) licensing, decisions on reimbursement and coverage of health technologies are essentially comparative. Therefore, in undertaking a series of decisions on individual technologies, the broader value for money perspective may be lost. This has been recognized by the Dental and Pharmaceutical Benefits Agency (TLV) in Sweden, where in addition to assessments on new drugs, is also undertaking a series

of reviews on existing products, covering 49 therapeutic groups. In order to achieve overall value for money, it is likely that NICE will also need to undertake similar reviews, either through its technology appraisal or clinical guideline programme.

HTA is continually evolving

The other recent change is that NICE has issued supplementary guidance on the technology appraisal of 'end of life' therapies. If the therapy is for a small patient group with a life expectancy of less than 24 months, therapies that add more than three months to life can be appraised differently. That is, the Appraisal Committee can decide that the value of the QALYs gained could be such that this would put the therapy below the willingness-to-pay threshold.

Thus, recent experience from the UK illustrates that HTA methods and processes are continually evolving. Different jurisdictions can learn from each others' experiences and it is important that we continue to compare and contrast the different approaches within Europe and elsewhere.

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Emergence of HTA in Central and Eastern Europe

Corinna Sorenson

Since the political and economic transition of the 1990s, extensive changes have transpired in the health sectors of several countries in Central and Eastern Europe (CEE)*. Such transformations have been marked by economic growth, ageing populations, advances in medical technology, and expanding expectations on the part of national populations. Widespread health care reforms and increased spending followed to address these changes, but this introduced new challenges to contain costs, improve the quality of services, and ensure rational and transparent spending decisions.

HTA serves as a potential tool to meet these aims and objectives. Its potential for contributing to more efficient, effective, and high quality health care is widely acknowledged in Europe and elsewhere, and is evidenced by the expanding implementation of national HTA systems. Even Members States without formal HTA systems are beginning to develop informal programmes or practices to inform policy making. Interest in HTA is certainly vibrant in the CEE region, as reflected in recently established systems in several countries, such as Hungary and Poland, and in wider discussions on the adoption of HTA-based approaches.

Emergence of and support for HTA in CEE

Hungary was the first country in the region to adopt the use of HTA in health care decision making, beginning in the early 1990s with the establishment of the Hungarian Coordinating Office of Health Technology Assessment. At present, almost all of the other countries have dedicated HTA bodies or they are currently under development or discussion. Most of these bodies assume an advisory role, where they assess the available evidence and make coverage and reimbursement recommendations to the Ministry of Health or other relevant ministry. Some bodies, such as the Agency for Health Technology Assessment in Poland (AHTAPol), also

* Bulgaria, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia, and Slovenia.

coordinate independent reviews by external organizations. Similar to other Member States, several countries, such as Latvia, Hungary, and Estonia, also have national HTA agencies that conduct assessments and issues reports, but are not directly involved in national decision making. However, in Hungary, advisory and national HTA entities often collaborate in reviewing health technologies.

To date, HTA programmes in CEE predominately focus on assessing the value of pharmaceuticals and less so of medical devices and other health technologies. This is especially true with regards to evaluating technologies for inclusion in the benefit basket.

In most CEE countries there has been notable stakeholder support for the implementation of HTA, especially from governments and patients or consumers. Despite such interest, there has been limited formal involvement of stakeholders in HTA processes. This may be a particular challenge for CEE countries, given that stakeholder engagement is resource intensive, as highlighted in the Overview article. However, some countries have been progressive in this area, involving various stakeholder groups in assessment committees, councils, and the like. For example, the Consultative Council of the AHTAPol entails a variety of external experts from governmental bodies, academic medical centres, universities, and health associations. The Council helps identify and prioritize reviews, assists in the review process, and provides comments on final decisions or reports. Several HTA bodies in the region also collaborate with international networks, such as the International Network for Agencies for Health Technology Assessment (INAHTA) and the European Network for Health Technology Assessment (EUnetHTA).

Adopting new methods to decision making

Poland, Hungary, and the Baltic States developed and implemented national HTA and/or pharmacoeconomic guidelines in the early 2000s, which provide direction to manufacturers, sponsors, and health care providers preparing health economic evaluations to support applications for public reimbursement.[1–3] They have been developed by these countries to ensure the provision of standardized, reliable, transparent and robust evidence to HTA and decision-making bodies.

In particular, all countries require and consider evidence on effectiveness, typically from randomized controlled trials (RCTs) and/or economic modelling. While most countries recommend that health economic information (specifically, cost-effectiveness) be submitted for assessment, only Poland, Hungary, Latvia, Slovakia, Lithuania, and Estonia explicitly require such evidence. Some countries (Bulgaria, Hungary, Latvia) only require economic evaluation for high-cost drugs. Health system impact analyses are often required to assess a technology's budget impact, its influence on health service organization, and any social and ethical issues.

Decision makers base adoption and funding decisions on a variety of criteria, but therapeutic benefit, cost-effectiveness, disease severity, availability of other treatments, and budget impact are the most important. Similar to other European countries with HTA systems, deciding on an appropriate (if any) cost-effectiveness threshold is an issue for countries in the region. At present, no country employs an explicit decision threshold. Some argue that an accepted threshold should be at or below the annual GDP per capita at purchasing power parity (PPP),[4] while others recommend three times the GDP per capita.[5] In the case of Hungary, for example, the application of the former argument would result in a threshold value of around €14,000/QALY. Other views and decision-making approaches suggest that no single threshold value should apply to all interventions or patient populations, and that a broader range of evidence should be considered.

Remaining challenges

Several challenges faced by CEE countries relate to capacity and available resources for HTA activities. As many of the HTA agencies are early in their establishment, they are faced with a lack of qualified personnel and funds to conduct assessments. This is compounded by the lack of educational and training opportunities in HTA in the region, especially in the Czech Republic, Slovakia, Lithuania, and Bulgaria. To address this issue, Poland engaged in a 'Twinning Project' with France between 2006 and 2008, where experts from France and other EU countries came together to review the HTA situation in Poland and hold workshops, trainings, study visits, and internships on economic evaluation, reimbursement processes, and the role of stakeholders. This provides a good example of how international collaboration can help support the implementation of HTA in lower-resourced countries. However, it is important that sufficient investment in HTA capacity-building also be made by individual CEE governments.

Another related challenge is setting assessment priorities. While HTA is mainly applied to drugs, there is significant opportunity to apply it to all health technologies. Countries with greater capacity and resource constraints should consider the total available budget, existing human capital (trained HTA evaluators), accessibility of data, appropriate methods, and the capacity of the health systems to use the results.[6] These factors can and should influence the number and range of assessments that can be conducted. Regardless of the approach used, topic selection should be as transparent as possible to ensure it is open, systematic, and unbiased, especially if not all technologies are reviewed. Countries should also aim to apply HTA to identify areas of disinvestment, where possible.

CEE countries also face methodological issues, with the availability of data being a central problem. Firstly, there has been a lack of systematic data collection on health status, outcomes, and costs in the region, leading to a paucity of national data and a greater reliance on studies from abroad. While clinical and epidemiological evidence is usually considered transferable, economic data is more context-specific. As such, economic studies cannot easily be imported from other countries, posing a significant challenge for

resource-limited countries.[7] The use of general models populated with local data may address these issues, albeit with some limitations.

Another option is to base priority-setting of assessments on products or interventions already evaluated by other systems. In this case, guidelines and training to adapt such studies are needed, in conjunction with greater international collaboration for openly sharing reports and methodological approaches. In particular, more guidance could be given to HTA producers on assessing and aggregating evidence from different sources, as well as its critical appraisal. Using fast-track or rapid assessments (see UK case study) may offer another viable option to make the best use of limited data and resources.

HTA offers an important tool to support governments and other stakeholders to obtain better value money from investments in health care. This is especially pertinent for CEE countries, which have limited resources and often burdened health systems. While challenges remain, much progress has been made to integrate the use of HTA in health care decision and policy making in the region. CEE countries should capitalize on the lessons learned from more established international HTA systems and adopt successful strategies implemented by these countries, where appropriate. Indeed, it is possible to learn from other jurisdictions' experiences, especially through international collaboration, while still applying measures that correspond with local circumstances. Doing so will not only better support the use of HTA in the region, but also strengthen the HTA enterprise across Europe.

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