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ORIGINAL PAPER

Health technology assessment in Poland, the Czech Republic, Hungary, Romania and Bulgaria

László Gulácsi · Alexandru M. Rotar · Maciej Niewada · Olga Löblová · Fanni Rencz · Guenka Petrova · Imre Boncz · Niek S. Klazinga

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Abstract This paper describes and discusses the development and use of health technology assessment (HTA) in five Central and Eastern European countries (CEE): Poland, the Czech Republic, Hungary, Romania and Bulgaria. It provides a general snapshot of HTA policies in the selected CEE countries to date by focusing on country case-studies based on document analysis and expert opinion. It offers an overview of similarities and differences between the individual CEE countries and discusses in detail the role of HTA by assessing its formalization and institutionalization, standardization of methodology, the use of HTA in practice and the degree of professionalization of HTA in the region. It finds that HTA has been to some extent implemented in all five countries studied, with methodologies in accordance with international standards, but that challenges remain when it comes to the role of HTA in health care decision-making as well as to human resource capacities of the countries. This paper suggests that coming years will show whether CEE countries develop adequate national analytical capacity to assess and appraise technologies in the context of local need and affordability, instead of using HTA as a mere administrative procedure to fulfill (inter)national requirements. Finally, suggestions are provided to strengthen HTA in CEE countries through cooperation, mutual learning, a common accreditation of HTA bodies and increased network building among CEE HTA experts.

Keywords Health technology assessment · Bulgaria · Czech Republic · Hungary · Poland · Romania

JEL Classification I 180

L. Gulácsi (✉) · F. Rencz
Department of Health Economics, Corvinus University of Budapest, Fővám tér 8., 1093 Budapest, Hungary
e-mail: laszlo.gulacsi@uni-corvinus.hu

A. M. Rotar · N. S. Klazinga
Department of Social Medicine, University of Amsterdam, Meibergdreef 9, 22660, 1100 DD Amsterdam, The Netherlands

M. Niewada
Department of Experimental and Clinical Pharmacology, Medical University of Warsaw, Żwirki i Wigury 61, Warsaw, Poland

M. Niewada
HealthQuest Consulting Company, 63 Mickiewicza Street, 01-625 Warsaw, Poland

O. Löblová
Department of Public Policy, Central European University, 1051 Budapest, Nádor utca 9, Budapest, Hungary

G. Petrova
Department of Social Pharmacy and Pharmacoeconomics, Faculty of Pharmacy, Medical University, Sofia, Bulgaria

I. Boncz
Institute for Health Insurance, Faculty of Health Sciences, University of Pécs, Mária u. 5-7., 7621 Pecs, Hungary

Introduction: health technology assessment in Central and Eastern Europe

Countries of Central and Eastern Europe (CEE) share a common past but have, since 1989, taken different routes in the organization and financing of their health care systems. All have undertaken various reforms in order to improve their health systems' performance. Health technology assessment (HTA) as a tool for informing decision-making on value for money of publicly reimbursed health technologies and their conscious introduction and use has been

one possible avenue to increase efficiency of health systems, one that many CEE countries have considered and to some extent implemented. Compared to a decade ago, there has been a significant increase of activity related to HTA for decision-making purposes in Central and Eastern Europe. In this paper we evaluate the developments in the field of HTA to date in five CEE countries (Poland, the Czech Republic, Hungary, Romania and Bulgaria), with a focus on its institutionalization, standardization of methodology, use of HTA in practice and capacity-building.

Materials for this paper were collected through document analysis and pooling of country expertise. Experts from all countries under study were involved in the systematic discussion of the situation in their country, based on a common set of questions. Country descriptions were further validated and refined through consultation with other CEE HTA experts and policy-makers as well as through discussions based on draft texts amongst the authors.

This article starts by describing the context of health care spending in the selected countries. Next, the HTA situation in the five countries is described, comparing the institutionalization, standardization and professionalization of HTA, as well as its use by decision-makers. Finally, an assessment of current issues with HTA in CEE is presented and suggestions are put forward for further progress of HTA in the region.

HTA in context: expenditure on health care in CEE countries

Economic situations, as well as spending on health care, vary among individual CEE countries (see Table 1). Similarly, pharmaceutical expenditure per capita and its growth rate (2003–2011) for these countries differ significantly (Fig. 1). There are countries such as Hungary with high per capita pharmaceutical expenditure and very high, sometimes double digit, yearly growth rates. Yearly growth rate was very high, for instance, in Romania (19.2 % from 2007 to 2008), although the starting level of per capita pharmaceutical expenditure was very low. Both per capita expenditure and its growth rate were stable in the Czech Republic in this period. The yearly growth rate was between 1.9 and 8.2 % in Poland, although Poland started from a low spending level and in 2011 its drug budget was still much lower compared to other CEE countries except Romania. Bulgaria is difficult to analyze due to lack of data.

Without suggesting any straightforward relationship between health care expenditure in CEE countries and the use of HTA in pricing and reimbursement decision-making, it is important to keep the diverse context in mind as we turn to a qualitative overview of the role of HTA in Poland, the Czech Republic, Hungary, Romania and Bulgaria.

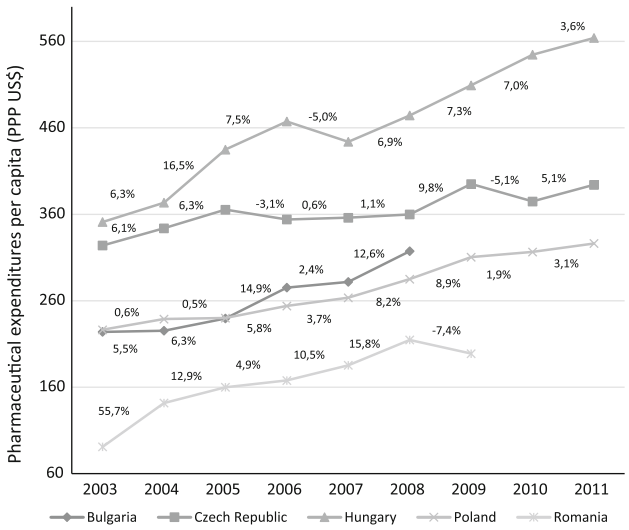

Fig. 1 Changes in pharmaceutical expenditures in US$ PPP per capita in CEE countries between 2003 and 2011 (or nearest year). Miscellaneous: pharmaceutical expenditures cannot be separated and include medical non-durables. *Sources*: OECD Statistics Database, Eurostat Statistics Database, available: 10/11/2013. http://epp.eurostat.ec.europa.eu/portal/page/portal/health/public_health/data_public_health/database. http://stats.oecd.org/Index.aspx

Table 1 GDP and expenditure on health care in CEE countries, 2011

Country	GDP per capita (current US$)	Total health expenditure per capita (current US$)	Total health expenditure (% of GDP)	Public health expenditure (% of GDP)	Private health expenditure (% of GDP)
Bulgaria	7,287	522	7.3	4	3.2
Czech Republic	20,580	1,507	7.4	6.2	1.2
Hungary	13,909	1,085	7.7	5	2.7
Poland	13,382	899	6.7	4.8	1.9
Romania	8,539	500	5.8	4.7	1.2

Source The World Bank DataBank, available: 16/11/2013
http://databank.worldbank.org/data/home.aspx

Poland

The Agency for Polish Health Technology Assessment (AHTAPol) was established in 2005 and published its first HTA guidelines in 2007. The current version of HTA guidelines was published in 2010 [1]. Additionally, the Minister of Health issued in April 2012 an official statement on the minimum requirements for HTA reports supporting reimbursement applications, setting of the official sales price or increasing the official sales price of a drug, a special purpose dietary supplement or a medical device [2]. Both the statement and HTA guidelines specify how to prepare the HTA report that is submitted to the Ministry of Health (MoH) and then transferred to AHTAPol, where the processes of assessment and appraisal take place and a statement by the expert Transparency Council (until 2011 known as the Consultative Council) is issued, followed by a final recommendation from the President of AHTAPol.

There is a standardized format for recommendations that currently covers: statement on public financing, justification, objective, health problem, description of technology, alternative technology, efficacy, safety, relation of cost to health effects, impact on payer budget, recommendation from HTA institutions from other countries, course of preparing the recommendation. Since 2009 AHTAPol has been an independent legal entity with its own budget, operating at the national level under supervision of the MoH. Manufacturers are obliged to pay a fee (€25,000) after every submitted reimbursement application. The AHTAPol team consists of around 60 qualified employees and the annual budget is about €650 000. AHTAPol assesses and appraises all medical technologies, drugs, devices, and other services (i.e. screenings or other health orientated programs funded through local authorities' budgets) that are claiming public funding. The role of AHTAPol covers the assessment and appraisal of HTA reports including scoping (definition of the decision problem), systematic review of clinical findings, economic evaluation, and budget impact analysis. An important issue is the cost-effectiveness threshold of 3 × GDP per capita/QALY (quality-adjusted life-year) that has been published in the Reimbursement Act and affects all medical technologies claiming public funding [3].

Statements of the Transparency Council, the President's recommendations and meeting proceedings are available on the AHTAPol website (http://www.aotm.gov.pl). The majority of reports are submitted by the pharmaceutical industry and prepared by consulting companies.

Between 1 January 2007 and 31 January 2014, 543 reimbursement recommendations were made: 516 on drugs and 27 on non-drug medical technologies.

There have been three reviews and evaluations of AHTAPol recommendations for drug therapies published so far [4–6]. Kolasa et al. evaluated the recommendations for drug therapies issued between 2007 and 2009 and assessed the impact for policy-making [4]. Altogether 151 recommendations of drug therapies were evaluated: the number of positive and negative recommendations was 88 and 63, respectively. The reasons for negative recommendations were: insufficient clinical data (32 cases), poor efficacy or safety (19 cases), unacceptable cost-effectiveness/cost-utility ratio (9 cases), an unacceptable budget impact (2 cases) and risk of off label use (1). From the 88 positive recommendations, 33 were classified as for use with major restrictions, 40 with minor restrictions and 15 without restrictions. A comparison of 67 recommendations issued in 2008 in Poland with the Scottish Medicinal Consortium's decisions [5] showed that among clinical reasons, inappropriate comparators were the most frequent cause of negative recommendations and rejections in Scotland; however, in Poland safety concern was one of the most often cited reason for rejection.

Another evaluation of the published AHTAPoL recommendations was performed and published by Niewada et al. [6]. All 344 recommendations completed before 7 October 2011 and available on the AHTAPoL website were analyzed: 218 positive (62.8 %) and 126 negative (37.2 %) recommendations. Clinical efficacy, impact of hard endpoints, safety, cost-effectiveness, and formal issues were explicitly discussed by the Consultative Council in 238 (69.2 %), 169 (49.1 %), 155 (45.1 %), 140 (40.7 %) and 47 (13.7 %) recommendations, respectively. Altogether, 106 (30.8 %) recommendations included cost/QALY and 193 (56.1 %) budget impact estimates. Negative recommendations ($n = 126$) were made due to unsatisfying and unfavorable results, most important arguments were: clinical efficacy (68 recommendations, 54 %), impact on hard endpoints (48, 38.1 %), safety (57, 45.2 %), cost-effectiveness (56, 44.4 %), budget impact (17, 13.5 %) and other formal issues (61, 17.7 %). No clear relationship was observed between cost-effectiveness and budget impact and positive or negative recommendations, while clinical aspects seem to be more important than economic ones. Clinical efficacy and safety profile were found to contribute most to the final recommendations. No empirical threshold value for cost-effectiveness and budget impact analyses that would separate positive and negative recommendations could be identified. Clinical efficacy and safety profile were found to contribute most to the final recommendations.

Czech Republic

The Czech Republic does not have a formal HTA body in the sense of an independent agency (such as AHTAPol in Poland) or a unit with the MoH (such as TAHD in

Hungary). The creation of an HTA agency was on the agenda of the Ministry of Health in 2013 [7] and several organizational setups were considered throughout 2012–2013 [8, 9]. The new minister of health (in office since January 2014) has so far not mentioned HTA as a policy priority and the fate of a future HTA body is now uncertain.

On the other hand, the State Institute for Drug Control [10, 11], which has been responsible since 2008 for pricing and reimbursement (P&R) decisions in the Czech Republic, has recently developed a certain interest in HTA, although the institute does not claim to do HTA per se but focuses rather on further developing and formalizing the use of pharmacoeconomics. SÚKL's future initiatives in the field could be affected by the dismissal of the institute's director in mid February 2014—the new minister of health expressed dissatisfaction with the institute's work on pricing and reimbursement and put forward that SÚKL should be "more flexible and under greater control of the state" [12].

P&R decisions are made by SÚKL in a joint procedure. The application dossier, mandatory for all new pharmaceuticals in order to be covered by public health insurance, must include a pharmacoeconomic analysis of cost-effectiveness and budget impact analysis in addition to clinical information and other elements required by law. Organizational, social and other issues considered by multidisciplinary HTA analysis are not taken into account by the institute.

Cost-effectiveness and budget impact analyses are typically carried out by the marketing authorization holder or consultancies; SÚKL enters only at the appraisal stage—which is, as the institute is not an HTA body with advisory functions but a regulator for P&R, identical with the decision-making phase. There is no separation of the appraisal/decision stages within SÚKL from an organizational point of view. SÚKL's decision-making style has been described as a "bureaucratic process" by some observers [13], with an emphasis on legal and formal transparency of procedures. SÚKL's P&R staff has mainly a legal or pharmacy and medical background, with little formal academic training in HTA, as there are no master's or doctoral study programs in the Czech Republic specialized primarily in HTA, and only a few which cover health economics, mainly at post-master level. SÚKL published, in October 2012, official guidelines for budget impact analysis and in February 2013 for pharmacoeconomic analysis, as well as checklists for both [10, 11]. Cost-utility analysis with QALY (or LYG) is preferred by the institute; only permanently reimbursed products can be in principle considered comparators.

The institute's decisions are publicly available on the internet and contain an overview of the dossiers as well as related reasoning. Typically, a decision would provide a detailed overview of the procedural and legal aspects as well as brief summaries of evidence provided by the applicants and used by SÚKL for appraisal. This evidence generally includes clinical and sometimes health economic publications in the Czech language or in English. Throughout the process, third parties (especially professional associations of specialists) can provide statements to inform the decision. Marketing authorization holders have the right to appeal to the Ministry of Health if they do not agree with a decision.

Unlike in Poland, there is no legally binding official financing threshold of cost-effectiveness requirement; SÚKL is merely required by Law 48/1997 Article 39b to take into account the drug's cost-effectiveness and budget impact. However, the institute did, in 2013, repeatedly mention in its decisions a "generally accepted willingness-to-pay threshold", set at the WHO-recommended 3 times GDP/QALY [14]. It is at this point unclear how strict the institute will be in denying reimbursement to drugs that fail to pass under the threshold. Drugs applying for reimbursement under the special category of "highly innovative medicinal products" are in any case exempt from having to prove their cost-effectiveness. Article 40 of Ordinance 376/2011 defines highly innovative medicinal products (*Vysoce inovativní léčivý přípravek,* VILP) by their clinical characteristics in considerable detail. In short, VILPs are products for severe diseases which either reduce adverse effects compared to existing treatment, offer clinical benefits for diseases without known effective therapy, or for which there is a lack of cost-effectiveness or real-life clinical outcomes data if available data points to benefits of the product compared to existing treatment. Regarding the temporary nature of reimbursement of VILPs, see also the April 2012 Opinion of the Ministry of Health on reimbursement of highly innovative products, which opens the possibility of longer reimbursement than the 3 years' maximum [15]. Drugs approved for reimbursement in the past have been known to surpass the threshold. This is especially true for orphan drugs [16]. The weight of economic considerations in SÚKL's decisions is unknown; to the best of our knowledge no study of its decisions has been done to this date.

We observe in the Czech Republic a hybrid situation: on the one hand, we see a body which is highly active, formalized and transparent in appraising cost-effectiveness. Moreover, this body has regulatory capacity and its appraisals of cost-effectiveness analyses are immediately translated into decisions—which is quite rare also in countries with longer traditions in HTA [17]. On the other hand, the body does not show significant interest in other aspects of HTA. For the moment, cost-effectiveness and budget impact analysis seem sufficient for decision-making purposes.

Hungary

The Office of Health Technology Assessment (OHTA) was established in 2004. OHTA, as an assessment and appraisal unit of the MoH has the task of providing an organizational framework for HTA that serves as the basis for the subsidy approval decisions of the National Health Insurance Fund Administration (NHIFA). OHTA performs assessments of drugs (since 2004) and medical devices (since 2007). In 2012, OHTA was integrated into the National Institute for Quality and Organisational Development in Healthcare and Medicines, and was re-named as Technology Appraisal Head Department (TAHD). TAHD carries out assessment, a formal procedure including the evaluation of the submitted economic dossier which is a legally required part of each company submission. In 2002, the Ministry of Health released guidelines for conducting health economic analyses which determine the methodological issues of health economic evaluations. The current version of the guideline was issued in 2013 [18]. In this guideline, technologies claiming for public funding are declared as cost-effective under the threshold of 2× GDP per capita/QALY, and proclaimed not cost-effective if the ICER is higher than 3× GDP per capita/QALY.

Between 2004 and 2010 altogether 997 company submissions were received by OHTA and evaluated by its staff and a further 250 were received and evaluated after 2011 until the end of 2013 [19]. Companies have to pay a contribution fee which is, for pharmaceuticals, under the normal procedure 1.5 million HUF (€5,068) per submission. Details on TAHD assessments, aspects of decision making and recommendations are not publicly available. The final reimbursement decisions made by NHIFA can be found on the NHIFA website. In 2004, 20 % of the submissions contained a health economic analysis, while in 2010 this rate was more than 80 % [19]. OHTA/TAHD published one systematic literature review (as partial HTA) about drug eluted stents [20]. Itemized funding refers to a case-based reimbursement of new medical technology when not hospitals but NHIFA buys the medical devices or medications (e.g. biological drugs) and high-value medical interventions (e.g. PET, CT) from manufacturers, finances them item by item according to protocol, and distributes them to hospitals for the treatment of selected patients. A reimbursement priority score card was introduced by a ministerial decree in 2010 for the evaluation of new hospital medical technologies financed through the DRG scheme or itemized funding [21].

Between 2010 and September 2013, 14 company submissions were assessed and appraisal decisions were made. Technologies included drug pumps, test strips, joint prosthesis, monochromatic polarized light, laboratory assays or a valve replacement system [22]. Recommendations and

Table 2 Reimbursement priorities for hospital medical technologies in Hungary

Priorities	Maximum number of points
I. Priorities of the health care system	*20*
I.1. National public health programs	6
I. 2. Health policy priorities	7
I. 3. Total health gain	7
II. Severity of the disease	*15*
II.1. Acute life-threatening disease	13–15
II.2. Chronic life-threatening disease	10–12
II.3. Acute non-life-threatening disease	8–9
II.2. Chronic non-life-threatening disease	6–7
III. Equity	*15*
III.1. Size of the target patient population	8
III.2. Accessibility	7
IV. Cost-effectiveness, quality of life	*30*
IV.1. ICER	15
IV.2. Health gain per patient	15
V. Budget impact	*10*
VI. Opinions from Hungary and abroad	*10*
VI.1. Professionals College in Hungary	3
VI.2. International experiences	3
VI.3. Available level of evidence	4
Total	*100*

Source 28/2010. (12/05/2010) Decree of the Ministry of Health in Hungary

I.1. *National public health programs* procedures gain points which promote one of the following public health actions: I.1.1. National Action Plan for Child Health, I.1.2. National Action Against Cancer, I.1.3. Hungarian National Cardiovascular Program, I.1.4. National Mental Health Program

I.2. *Health policy priorities* I.2.1. Procedures that improve efficiency of the health care system, I.2.2. Procedures that reduce or substitute the length of hospital stay, I.2.3. Telemedicine: use of telecommunication in health care service, I.2.4. Minimally invasive or non-invasive procedures, I.2.5. Procedures that promote rehabilitation, I.2.6. Treatments that affect the etiology of the disease not symptomatic treatments, I.2.7. Preventive care

I.3. *Total health gain* considering QALYs, DALYs or life-years gained, a procedure with high societal QALY or life years gained or low DALY receives more points

II. *Severity of the disease* acute life-threatening diseases gain more points and chronic non-life-threatening diseases fewer points

III.1. *Size of the target patient population* the smaller patient population gains more points. III.2. *Accessibility:* procedures gain more points which are available across the whole country

IV.1. *ICER* incremental cost-effectiveness ratio, IV.2. *Health gain per patient*: considering QALYs, DALYs or life-years gained per patient, a procedure with high societal QALY or life years gained or low DALY receives more

V. *Budget impact* procedures gain more points that result in smaller outflows or larger savings in the National Health Insurance Fund

VI.1–2. *The College of Professionals in Hungary; International experiences* professional opinions and international experiences must be considered, VI.3. *Available level of evidence* according to the hierarchy of evidence, the highest evidence gains 4 points and the levels beneath count 0.5 point less per level

Table 3 Technology assessment criteria Romania

No.	Criteria	Points
A	*Results of HTA evaluation HAS, France*	
A1	SMR I-II	1
A2	SMR III-IV	0.5
A3	Therapeutic value is insufficient	0
B	*Results of HTA evaluation NICE, SMC, AWMSG, United Kingdom*	
B1	Approved reimbursement without restriction	1
B2	Approved reimbursement with restriction	0.5
B3	Not reimbursed	0
C	*Reimbursement status in EU*	
C1	Reimbursed in minimum 16 and maximum 24 EU countries	2
C2	Reimbursed in minimum 11 and maximum 15 EU countries	1.5
C3	Reimbursed in minimum 6 and maximum 10 EU countries	1
C4	Reimbursed in minimum 1 and maximum 5 EU countries	0.5
D	*Relative efficacy*	
D1	Superior relative efficacy vs comparator/active comparator or placebo	2
D2	Non-inferior relative efficacy vs comparator/active comparator or placebo	1
D3	Lower relative efficacy vs comparator/active comparator or placebo	0
E	*Relative safety*	
E1	Lower side effects vs comparator/active comparator or placebo	2
E2	Similar/equal side effects vs comparator/active comparator or placebo	1
E3	More side effects vs comparator/active comparator or placebo	0
F	*Patient reported outcomes*	
F1	Superior PRO vs comparator/active comparator or placebo	2
F2	Similar/equal PRO vs comparator/active comparator or placebo	1
F3	Lower PRO vs comparator/active comparator or placebo	0
	TOTAL	10

SMR (Service Médical Rendu – therapeutic value) index classifies the importance of an intervention such as major (I), important (II), moderate (III), weak (IV), and insufficient to justify a reimbursement (V). (http://www.ispor.org/htaroadmaps/france.asp)

HAS Haute Autorité de Santé, *NICE* National Institute of Clinical Excellence, *SMC* Scottish Medicines Consortium, *AWMSG* All Wales Medicines Strategy Group

results of these appraisals are not publicly available. In this priority scoring system, the maximum achievable score is 100 (Table 2). Scoring is done by NHIFA, technologies reaching 60 points become potential candidates to be financed through DRG. Technologies are to be financed if they receive at least 60 points and reach at least 40 % of achievable points of all the six criteria.

Romania

Pharmaceutical expenditures were growing rapidly over the past decade in Romania, until the financial crisis of 2008 (Fig. 1). This persistent growth became one of the concerns of the external creditors of the Romanian government, the International Monetary Fund (IMF) and the World Bank (WB). Following their suggestions, the government expressed its engagement in initiating development of HTA by the end of 2011 as a cost containment mechanism [23]. As a result, the Romanian government, financed by the WB, contracted as consultants NICE International (UK) to provide recommendations on how to reform the health care system. Among others (e.g. the revision of the basic benefit package), the advice was to create a de facto HTA process in order to increase the transparency and efficiency of decision-making [24, 25].

On 24 April 2012, the Romanian government made the first step in embedding HTA in health care governance. The first phase was to create a legal framework, followed by the development of a methodology and a submission process only for new drugs. The legal framework for HTA was created through Government Decision 351/2012, which was an amendment of a previous Government Decision 144/2010, regarding the organization and function of the MoH [26]. As a result of this legislation, an HTA unit was set up within the MoH in late 2012. The mandate of the HTA unit, introduced by the legislation, is broad: HTA can be applied to all existing medical technologies such as pharmaceuticals, medical devices, health policies and public health. According to an HTA guideline, published in 2013 by the MoH [27], the assessment of innovative drugs is made using a 6-item scoring chart

where the maximum number of points is 10, and for a positive reimbursement recommendation, the pharmaceutical product has to score at least 6 (Table 3).

Based on Table 3 we can conclude that the decision on reimbursement is reached by assessing two distinct types of evidence:

- Reimbursement recommendations given by HAS, France, and 3 HTA bodies in the UK (NICE/SMC/AWMSG), and reimbursement status in other EU member states;
- Clinical profile of the intervention: relative efficacy, relative safety and patient reported outcome (PRO) [28].

In the scoring scheme, all items have equal weights and none of them represent a knock-out criterion. Apart from the documents referring to the 6 scoring criteria, budget impact data is required in the reimbursement dossier. However, this has the role only of informing the decision-maker on the potential total expenses of a given technology and does not influence the final scoring. Supporting documentation has to be submitted according to a required structure which is critically assessed by means of a checklist. Both the structure and the checklist are adapted from the tools developed by the Canadian think-tank EVIDEM [29].

The supporting documentation has to be submitted to MoH and received by the HTA unit and the Specialty Committees. The HTA unit reviews all the documentation, French (HAS) and UK (NICE/SMC/AWMSG) HTA reports, the reimbursement status of the given drugs in EU countries, the clinical efficacy, safety, PRO data and analyzes the budget impact. Specialty Committees review only clinical efficacy, safety and PRO. The final scoring consists of an average of the grading given both by the HTA unit and the Specialty Committees.

Biosimilars are assessed slightly differently. For a positive recommendation they need to be accepted already for reimbursement in a certain number of EU countries, out of the number of countries where the product is marketed. The maximum price for which they can apply is set by law to a maximum 80 % of the original INN (International Nonproprietary Name) price.

By August 2013 the MoH published a list of 167 dossiers received [30]. According to law, all these applications were supposed to be assessed and followed by a final recommendation in a maximum of 55–60 days after the day of application. In reality, this timeline was more than doubled. On 15 November 2013, the MoH started to publish its appraisals with the commitment for the rest to come in the following weeks [31]. By late December, the reviews of the HTA unit and the Specialty Committees for all 167 dossiers received by August were published. This was followed shortly by a report of the National Committee, summarizing the appraisals, which also included the decision of the final reimbursement recommendation and the need for prescription guidelines and restrictions [32]. Additionally, a new element was included in this document: "conditional reimbursement" for 12 months. In this timeframe, the manufacturer should collect and submit data from health economics analysis and budget impact. However, there are no guidelines or specific requirements as to how to satisfy this requirement.

Bulgaria

The pricing and reimbursement processes are controlled by the National Pricing and Reimbursement Council (NPRC) which is responsible for the inclusion and exclusion of pharmaceutical products on the Positive Drugs List (PDL), as well as its amendments. The NPRC, responsible for HTA assessment and appraisal, was established in April 2013 by the Council of Ministers and has its own budget, as well as nearly 40 employees. NPRC decisions are based on legislative requirements of the Law for Medicine [33], the Health Insurance Act [34] and related regulations [35]. Overall inclusion in PDL takes at least 60 days. Adapted or locally prepared pharmacoeconomic analysis as well as budget impact analysis must be part of the company submission. No HTA guidelines have been published yet. Company submissions received by NPRC are assessed by external experts in pharmacoeconomics, appointed by the minister of health.

Current requirements for gaining reimbursement are: (a) a registered price in Bulgaria, (b) a positive reimbursement decision in at least in 5 EU countries (c) favorable results from pharmacoeconomic analysis submitted with the application.

Only medicinal products included in the PDL can be reimbursed by public funds. Once a product has a marketing authorization it must have its price registered, for OTC products, or regulated, for prescription medicines. Pharmaceutical products for retail sale are subject to maximum prices registration. The maximum price of a prescription product (referred to as "approved ceiling price") is subject to regulation and approval by the NPRC. To obtain approval, the manufacturer or holder of the marketing authorization must submit to the NPRC an application detailing the elements included in the ceiling price. The application form is available on the site of the NPRC. The level of payment for medicinal products with the same INN and the same formulation reimbursed by NHIF is determined by the abovementioned HTA criteria. Clinical efficacy, safety data and results from health economics analysis are taken into account. Submissions are evaluated by the Pricing and Reimbursement Committee:

Table 4 Comparison of HTA in 5 CEE countries

	Poland	Czech Republic	Hungary	Romania	Bulgaria
1. Formalization and institutionalization					
Legal enforcement of HTA	2004	No	2004	2013	2013
Organization embedding	AHTAPoL	No HTA body; SÚKL	MoH, TAHD	MoH	NPRC
Human resource capacity (HTA)[a]	60 People	No HTA specialists	12–14 People	2 People	1–2 People
Technologies assessed	Pharmaceuticals, medical devices and all other medical services claiming public funds	Pharmaceuticals	Pharmaceuticals, medical devices, hospital medical technologies	Pharmaceuticals, medical devices, medical imaging technologies, and all other medical services claiming public funds	Pharmaceuticals, medical devices
2. Standardization					
Official HTA guideline development	AHTAPoL	SÚKL	TAHD (MoH)	HTA unit (MoH)	NPRC
Economic evaluations	CEA/CUA/BIA	CEA/CUA	CEA/CUA/BIA	CEA/CUE/BIA	CEA/CUA/BIA
Local data requirements	Yes	Yes	Yes	Yes	Yes
Criteria for positive recommendations	Efficacy, safety, ICER less than 3× GDP/capita, BIA and risk of off-label use	ICER ≈3× GDP/capita	Efficacy, safety, ICER less than 2–3× GDP/capita, BIA	HAS, NICE/SMC/AWMSG recommendation, reimbursement status in EU, relative efficacy and safety, PRO	Expert opinion
Public health priorities	Yes	Yes	Yes	Yes	Yes
Public health priorities linked to decision making	No	No	Yes for hospital medical technology	No	No
3. Execution					
Application fee	Yes	Yes	Yes	No	No
National/regional HTA process	National	National	National	National	National
Number of decisions	870	NA[b]	997 (2004–2010) and 250 between 2010 and 2013	167	271
Number of decisions on drugs	742	NA[b]	NA	167	271
Number of positive decisions on drugs	547	NA[b]	NA	130	NA
Published appraisals	870	NA	No	167	No
4. Further professionalization					
Shortage in trained professionals	Yes	Yes	Yes	Yes	Yes
Academic educational training	Yes	Yes	Yes	No	No

[a] Professionals responsible for HTA

[b] SÚKL's decisions are mandatory for any change of P&R for all pharmaceuticals

the decision is based on experts' opinion. Since its establishment, the NPRC has assessed 271 medicines included in the PDL; detailed reports are not publicly available.

Discussion

In all five CEE countries studied, HTA activities have been developed and have become internalized in the decision-making processes on technologies over the past decade. However, there are important similarities and differences. Table 4 summarizes the main characteristics. It groups the characteristics by level of formalization and institutionalization (legislation, official institutes with HTA tasks and their embedding in the health care system), by nature of the standardization (HTA guidelines, standard methodology, national criteria for decision-making), by execution (number and types of decisions made) and by professionalization (capacity building).

Formalization and institutionalization

HTA has been embedded in the law of four countries, in Hungary and Poland in 2005 and in Romania and Bulgaria in 2013. The Czech Republic has no legal embedding of HTA but CEA and BIA are mandatory requirements. Each of the countries studied has an HTA body: one (AHTAPol) is a legally independent organization with its own budget and a staff of 60 professionals, another (SÚKL) has no separate HTA capacity, while the other three are relatively small units with 2–4 HTA professionals within the health care ministry or national insurance institute. Only the Polish and Hungarian HTA bodies are members of INAHTA, although representatives from all five countries participate in the current EUnetHTA Joint Action 2 as well as in the European HTA Network established in 2013 by Directive 2011/24/EU on cross-border health care.

In all five countries HTA bodies play a role in the decision-making process, although their importance and competences vary. Stages of assessment and appraisal (in the sense of evaluation and recommendation, respectively, as understood in the UK context by NICE) [36] are more or less intertwined, with most bodies producing recommendations (appraisals) based on a review of company submissions rather than in-depth assessments; the procedure seems to have more of a technical administrative nature. Only reports provided by the Polish AHTAPol and the Hungarian TAHD contain de novo analyses. Final decisions are typically made by the ministry of health, with the exception of the Czech Republic where SÚKL's decision is binding unless appealed against.

Pharmaceuticals and medical devices are the most frequently assessed technologies. In most of the countries all medical services claiming public funds are subject to HTA, in some countries management and policy tools are included as well. The status of vaccines is somewhat different: they are considered as any other drug and the normal rules of HTA assessment and appraisal apply in Bulgaria and Poland, while in Hungary and Romania HTA assessment and appraisal is not required.

Standardization

HTA guidelines are provided to industry as a guide to create company submissions and are comparable in the CEE countries. Guidelines are also very similar to the ones in other EU countries, methodology is standardized and there is no important difference between old EU member states and CEE countries.

Guidelines require information about clinical efficacy and safety of the new medical technologies, systematic reviews, meta-analysis (mainly drugs), epidemiology of the given disease, disease burden, results from health economics analysis and patient reported outcomes. Local data are required to be used in industry economic dossiers for submissions. However, there is limited experience in most of the countries in analyzing published RCTs or other results (patient level study data from trials is not required in CEE countries). There is a shortage of input data to local health economics analysis (costs, unit costs, heath status, QoL). Only a limited number of registries that can be used as a local data-sources are maintained; in several cases insurance databases are used as quasi-registries.

Results from health economics and HTA from other countries, especially England (NICE) are used, however, HTA guidelines do not provide methodological support on how to adapt and transfer these results to CEE jurisdictions. Transferability of HTA results between countries implies the question as to what kind of data on effectiveness and costs can be transferred from one country to another. Up to now, data from clinical trials have been widely used in many countries without national/local participation in the trial. Hence findings on efficacy in trials might in practice have different levels of effectiveness in different countries depending on the functioning of the health care system. Epidemiological data like incidence or mortality might also be different among countries; however, their transfer is accepted in many cases. Cost data seem to be the most country specific issue, which means that applicants must use country specific cost data in the submission. However, due to the large number of submissions this is not a realistic requirement either. Available data have to be used; if the data is from a similar country in terms of economic development and overall funding levels in health care, as for instance from Poland to Hungary, this might be easier; if data comes from NICE or another Western European

agency, a sophisticated methodology is needed to transfer data in a valid way to the local context.

These transferability issues are all the more pressing where there is no link between public health priorities and reimbursement decision-making. Although four out of the five countries state that their country has specific public health priorities, it is far from clear how this influences the decision-making process for reimbursement of technologies.

There are differences in the criteria for positive recommendations in CEE countries related to safety issues, implementation of financing thresholds and the importance of reimbursement status in other countries. Safety issues are important and have a greater influence on reimbursement decisions in Poland than perhaps in other countries in Europe [5]. The quality of clinical trial evidence, used by the Food and Drug Administration (FDA) varied widely across indications, the effectiveness and safety of newly approved therapeutic agents might not be well understood [36]. A similar review has not been published yet about the clinical trial evidence used by the EMA; however, the findings might be generalizable regarding EMA. Due to the shortage of registries, the capacity to control safety problems in the CEE might be weaker than in developed countries. As with effectiveness and costs, it is unclear whether safety findings from other countries can be safely transferred to the situation in CEE countries. The financing threshold is also an important issue: a 3× GDP/capita threshold was implemented officially in Poland and in Hungary, and tends to be used in the Czech Republic, Romania and Bulgaria. Providing all drugs under the threshold and none above might be an attractive decision-making approach due to its simplicity. However, despite the existing academic consensus, thresholds alone are not sufficient for assessing the interventions' value for money, and a series of other important factors have to be taken into consideration [37–39]. It is unclear how flexible or rigid the approach of CEE decision-makers will be with regards to thresholds.

Reimbursement decisions from other countries, mainly from NICE, are taken into consideration in all CEE countries studied. Officially, Romania declared in its HTA guidelines that reimbursement decisions are based on decisions from four HTA agencies (UK and France) and reimbursement practice in other EU member states. On the one hand this might be a good strategy if the main aim is to avoid major mistakes in reimbursement decisions; on the other hand, if the drug is cost-effective and reimbursed (for whatever reason) in France and in the UK it does not imply that this drug is cost-effective in Romania and, what is even more important, if the given drug is cost-effective in Romania it does not mean that this drug is really needed given the national public health priorities or, if needed, is necessarily fundable from public sources. In countries like England or France the final coverage decisions are the results of lengthy negotiations with industry and are not necessarily applicable in other countries with different economic and health care contexts.

If the aim is to maximize value in health care in CEE countries there is another topic that needs attention: drugs already under the reimbursement scheme, the "old drugs". Copies of products which were patented before 1988–2000 are still available on CEE markets and represent an important share in the turnover of domestic manufacturers. Some products have been deleted from the list of available drugs, usually at the request of the manufacturers. A number of these drugs were never evaluated and their effectiveness and cost-effectiveness are unknown. According to some studies from Hungary, even the clinical efficacies of some of these drugs are clearly lacking or questionable, yet these drugs are still reimbursed with significant budget impact [40]. The economic evaluation of old drugs presents a major challenge for HTA bodies in CEE countries. Many of these drugs were never internationally marketed or are no longer marketed in other EU countries. As a consequence, no good quality clinical evidence is available on the efficacy of these drugs, or the available evidence is 20–40 years old. It is also unlikely that clinical trials will ever be conducted for these drugs by either pharmaceutical manufacturers or governments [41].

In summary, standardization of HTA in the countries studied seems very much in line with the international methodological approaches towards HTA. However, the tendency to build HTA on effectiveness, safety and cost data and even norms that stem from more advanced HTA agencies in Europe has its limitations, and transferability should be assessed carefully. Furthermore, linkage to national public health needs and assessment of "old drugs" needs more attention.

Execution

In all five countries a large number of company submissions are regularly assessed and many appraisal decisions are made. This large number refers to various administrative procedures: one drug can be assessed for more than one indication and also already reimbursed drugs can apply for reimbursement for new indications. An evaluation of the functioning of this process in practice has only be performed and published in Poland. Poland also seems the most transparent in the publication of the details of appraisal reports in the public domain.

In the Czech Republic, SÚKL does not carry out assessments, only appraisal decision-making. The process is relatively transparent (decisions are available online and include reasoning) and there are official guidelines. In the

other countries processes focus on the assessment and appraisal of dossiers submitted by industry and although the methodology has been standardized, transparency on the actual execution of the assessment and appraisal can still be improved.

In all countries the focus in the execution seems to be on the administrative procedures of assessment and appraisal and only limited resources seem to be available to assess transferability of effectiveness, safety and cost data from elsewhere and/or de novo analyses with local data. Hence the danger lurks that HTA in CEE countries remains reduced to a merely technical administrative process based on a rationale that has not been fine-tuned for the national context.

Professionalization

Although all five countries have academics and civil servants who are knowledgeable and have been trained in the field of HTA, the overall capacity is still limited. Three of the five countries (Poland, Czech Republic and Hungary) have started training schemes to increase the number of HTA professionals. Whether the human resource capacity in a given country is sufficient or not is difficult to judge. Professionals with some knowledge in HTA are employed by MoHs, consultancy agencies, pharmaceutical companies, and academic institutions. Professionals are hired from other countries as well. From a comparative perspective, though, Poland is clearly best equipped in terms of human resources whose number seems to be proportional to fulfill the mission of AHTAPoL.

However, more important than training and headcounts of professionals as such is the question of whether HTA in CEE countries will develop in scope and depth in the direction of the performance of national analytical studies based on local data and the national context that reflect a reliable and valid approach towards value creation. This will depend on whether HTA is merely an administrative procedure, checking submissions from industry against a set of criteria, or includes de novo execution of analyses grounded in local context. In addition, the future of HTA will depend on how seriously policy-makers take HTA conclusions and how evidence-based policy processes in health care overall take place. A negative scenario is an HTA practice fuelled by industry with little counterbalancing power by health care administrators and policy-makers, resulting in a bureaucratic decision-making process copying results from elsewhere that have not been validated for the local context. A positive scenario is further professionalization of both government HTA staff and awareness of policy-makers, resulting in transparent decision-making processes through which evidence from industry is weighed systematically against societal values and priorities furnished by national studies based on local data.

Conclusion

Health technology assessment has, over the past decade, been developed and implemented in Poland, Hungary, Romania, Bulgaria, and to some extent also in the Czech Republic. These five CEE countries have formal requirements for HTA and HTA institutes, although organizational embedding, size and importance for decision-making differ. Standards for HTA are largely modeled after international examples. However, after the first phase of formalization, institutionalization and standardization, HTA in CEE countries now seems to be at crossroads. It can remain a technical administrative exercise to assess and appraise technologies using effectiveness, safety and cost data which comes from elsewhere and whose transferability can be questioned. It can also develop further to a more robust form of HTA where local data serve increasingly as input for analysis and where decisions are grounded in national priorities and values.

To achieve the latter, the following actions can be considered. First, local data on effectiveness, safety and costs could be shared amongst CEE countries. It can be expected that these data will increasingly become available and, given the similarities between CEE countries in economic development and health care systems, sharing of the data would enhance transferability compared with the present situation. Second, a common training of HTA staff might ensure that stress is put on insights and methodologies which are presently needed in order to bring HTA in the region to the next phase. Third, a mutual assessment and recognition of HTA bodies through certification or accreditation might be considered. Of course, this depends on whether countries agree on developing their HTA to a more mature level, but an international form of assessment and recognition, as exists in other areas such as the accreditation of accreditation organizations for hospitals as run through the International Society for Quality in Health Care, is worth considering. Lastly, it is important that HTA experts in CEE countries form their own community and exchange their knowledge and experience, which has accumulated over the past years by active participation in international HTA initiatives, including notably the EUnetHTA and EUROREGIO II initiatives: out of the 40 partners of the current EUnetHTA Joint Action 2 (2012–2015), 11 are from CEE countries. These are health ministries, national schools of public health, quality and accreditation institutes, and an HTA agency (AHTAPol). Strengthening of the network of HTA experts in CEE countries should

facilitate knowledge sharing and promote a more rigorous and robust approach to HTA in the region.

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