Title page

Title: **EQ-5D in Central and Eastern Europe: 2000-2015**

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Abstract

Objective: Cost per quality-adjusted life year data are required for reimbursement decisions in many Central and Eastern European (CEE) countries. EQ-5D is by far the most commonly used instrument to generate utility values in CEE. This study aims to systematically review the literature on EQ-5D from eight CEE countries.

Methods: An electronic database search was performed up to July 1, 2015 to identify original EQ-5D studies from the countries of interest. We analysed the use of EQ-5D with respect to clinical areas, methodological rigor, population norms and value sets.

Results: We identified 143 studies providing 152 country-specific results with a total sample size of 81,619: Austria (n=11), Bulgaria (n=6), Czech Republic (n=18), Hungary (n=47), Poland (n=51), Romania (n=2), Slovakia (n=3) and Slovenia (n=14). Cardiovascular (20%), neurologic (16%), musculoskeletal (15%) and endocrine/nutritional/metabolic diseases (14%) were the most frequently studied clinical areas. Overall 112 (78%) of the studies reported EQ VAS results and 86 (60%) EQ-5D index scores, of which 27 (31%) did not specify the applied tariff. Hungary, Poland and Slovenia have population norms. Poland and Slovenia also have a national value set.

Conclusions: Increasing use of EQ-5D is observed throughout CEE. The spread of health technology assessment activities in countries seems to be reflected in the number of EQ-5D studies. However, improvement in informed use and methodological quality of reporting is needed. In jurisdictions where no national value set is available, in order to ensure comparability we recommend to apply the most frequently used UK tariff. Regional collaboration between CEE countries should be strengthened.

Keywords: EQ-5D, health-related quality of life, value sets, health technology assessment, cost-effectiveness analysis, Central and Eastern Europe
Introduction

Over the past decade health technology assessment (HTA) has been implemented in most Central and Eastern European (CEE) countries based on methodologies of international standards [1]. These countries have formal HTA organisations involved in reimbursement decision making of health technologies. To support reimbursement decisions, cost-effectiveness analyses, or rather cost-utility analyses, in which quality of life or quality-adjusted life year (QALY) is the preferred outcome measure, are required in many CEE countries 2-8. Currently in the Czech Republic, Hungary, Poland and Romania, health interventions are deemed to be generally accepted if their incremental cost per QALY gain is not greater than 3 times the country’s GDP per capita [9,10,2].

The EQ-5D is by far the most commonly used preference-based instrument to calculate utility scores in CEE [11]. The main advantages of EQ-5D are its widespread use, briefness and the simplicity of administration. Official language versions are available for all the national languages of CEE countries. On the contrary, only very limited data is available from CEE countries using other preference-based measures such as SF-6D [12-14] and Health Utilities Index (HUI) [15] or directly measured utilities such as time trade-off or standard gamble [16-19]. Of note, HUI has not been validated in the national languages of CEE countries with the exception of Austria.

HTA bodies in the UK (National Institute for Health and Care Excellence, NICE) [20] and the US (Washington Panel on Cost-Effectiveness in Health & Medicine) [21] recommend using utilities obtained by indirect measures in cost-utility analyses. These recommendations were adopted by Hungary, Poland and Romania, which have included the EQ-5D as a preferred instrument in their HTA guidelines (Table 1) [24]. In Austria, the latest HTA guideline also recommends indirect methods of utility elicitation but without a specific recommendation of the EQ-5D [5]. In Slovakia, in contrast, direct methods are required [3], whilst in other CEE countries there is no preferred choice of instrument to derive utilities [5,6,22,8,7]. Little is known, however, about how far CEE countries have actually used the EQ-5D.

Prior systematic reviews have been conducted on various fields related to the use of EQ-5D including psychometric properties of the measure (e.g. minimal clinically important difference or responsiveness to clinical change) [23-25], EQ-5D valuation studies [26] and a
number of prevalent disease areas [27-36]. Nonetheless, the real-life use of EQ-5D in terms of geographical regions and as a proxy to HTA has not been reviewed to date.

The purpose of this study is, therefore, to systematically review the published literature on EQ-5D from selected CEE countries, namely Austria, Bulgaria, the Czech Republic, Hungary, Poland, Romania, Slovakia and Slovenia. Specifically, we aim to discuss the following issues:

- What has been the growth and composition of the literature on the EQ-5D in CEE?
- In which clinical areas has the EQ-5D been used in CEE?
- What are decision-makers' guidance on the approach for estimating utilities and does the literature match these?
- What is the quality of the studies and study reporting?
- What could/should analysts do in situations where there is no national value set and what are the implications of the various options?
Methods

EQ-5D

The EQ-5D questionnaire is a descriptive system that focuses on five health dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression \[37,38\]. Three versions of the instrument have been developed: a 3-level (EQ-5D-3L), 5-level (EQ-5D-5L) and a youth version (EQ-5D-Y) for children and adolescents aged 7 to 12 years \[39-42\]. In the EQ-5D-3L, each dimension has three response categories (representing no problems, some problems and severe problems), whereas in the EQ-5D-5L, responses may be one of five levels of severity (no problems, slight problems, moderate problems, severe problems, extreme problems). EQ-5D index scores can be attached to each health state description by applying societal preference weights to the self-report provided by the respondent. A number of value sets have been developed based on preferences of the general population elicited using a direct method such as time trade-off and EQ-5D visual analogue scale. In addition to the descriptive self-classifier, the EQ-5D contains a 20 cm visual analogue scale (EQ VAS) ranging from 0 (worst imaginable health) to 100 (best imaginable health) along which the respondents rate their current health.

Data collection

We followed the PRISMA checklist for reporting systematic reviews in our study \[43\]. A database search was performed using MEDLINE via PubMed, EMBASE, Web of Science, CINAHL, PsycINFO and The Cochrane Library up to July 1, 2015. We also conducted a search of the EuroQol Group database to identify additional studies with EQ-5D. The search strategy used the combination of the following terms: (euroqol OR euro qol OR eq5d OR eq 5d OR eq-5d) AND (Austria* OR Bulgaria* OR Hungar* OR Czech OR Poland OR Polish OR Romania* OR Slovak* OR Sloven*). Reference lists of articles identified through computerised search were also reviewed for relevant studies. Pooling their country expertise, the authors also hand searched for further papers from their own countries, which were published in journals not indexed in electronic databases. There were no language restrictions.

Articles were included in this review if they met the following criteria: i) full-text published paper; ii) represented an original research; iii) the study population originated from Austria, Bulgaria, the Czech Republic, Hungary, Poland, Romania, Slovakia or Slovenia; and iv) the
article reported EQ-5D measurement (psychometric) properties or scores on the EQ-5D index or EQ VAS or percentage dimension scores from either the adult or paediatric population. When interim or multiple studies reported data on the same patient population, only one paper was included, preferably the one which had a larger sample size. Multi-country studies, where EQ-5D outcomes of the CEE countries were not reported separately from other countries, were excluded.

Study abstracts that potentially met the inclusion criteria were identified, and full-text articles were retrieved for further review. Articles were assessed for eligibility by two independent investigators (F.R. and L.G.) with any disagreements resolved by discussion or a third researcher (M.P.).

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.

**Data extraction**

A Microsoft Excel spreadsheet was developed to collect data from the identified studies. This covered general characteristics of the papers (year of publication, language and funding source), methodological features of the study (method of data collection, design, setting and study year), characteristics of the study population (patients/general population, diagnosis and sample size), version of the questionnaire (EQ-5D-3L or EQ-5D-5L or EQ-5D-Y), tariffs used, mean EQ-5D index scores, mean EQ VAS scores, percentage dimension scores and total number of utilities (when EQ-5D index scores were stratified by subgroups, e.g. age, clinical types, severity) reported in the paper. Only participants who completed the EQ-5D were included in the sample size for studies. Diagnoses were classified according to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) [44].

**Results**

**Search results**

Results of the study selection process and reasons for exclusions are detailed in Figure 1. The electronic search of databases identified 108 articles that fulfilled our predefined inclusion
An additional 35 papers were found through hand searching by the authors, resulting in a total of 143 papers. Two of them were large European multi-country studies that involved more than one CEE country [45, 46]. Overall 152 reports on country level results were obtained: Austria (n=11) [47-57], Bulgaria (n=6) [45, 46, 58, 59, 13], Czech Republic (n=18) [60, 61, 45-46, 62-66, 20, 67-74], Hungary (n=47) [11, 75, 76, 45, 77-93, 14, 94, 18, 95-116, 12], Poland (n=51) [117, 118, 45, 46, 119-165], Romania (n=2) [45, 46], Slovakia (n=3) 166-168, and Slovenia (n=14) [169-178, 45, 46, 179, 180].

**Characteristics of the studies**

Main study characteristics are displayed in Table 2. The first EQ-5D studies in CEE were published from Slovenia (2000) [170], Hungary (2001) [114], Austria and Poland (2003) [51, 181], followed by Slovakia (2004) [168], the Czech Republic (2007) [70, 71], Romania (2013) [45] and Bulgaria (2014) [13]. In the past 15 years, the number of publications has steadily increased in the region (Figure 2). Two-thirds of the studies were published in English (n=97; 68%) and all non-English papers had an English abstract. The largest number of non-English articles was observed in Hungary (n=18; 38%). However, the highest rate of non-English reports within a country was found in the Czech Republic (n=8; 44%). Overall 105 (73%) studies stated the source of funding. The lack of a funding statement was most prevalent in Poland (n=22; 43%).

The majority of the studies had a cross-sectional design (n=85; 59%). For longitudinal studies (n=55; 38%), the length of follow-up ranged from 10 days [171] to 9.5 years [51]. Registry-based studies (n=3) were identified only in the Czech Republic and Hungary [77, 64, 174]. Almost all studies (n=126; 88%) were conducted as an on-site survey using a paper-based questionnaire. In addition, we identified six online or e-mail [118, 80-82, 182, 173] and six postal surveys [86, 95, 53, 123, 174, 180]. In three studies patients were permitted to complete the questionnaire at home and return it later [91, 170, 179].

Total sample size of all studies from the eight countries was 81,619 with Poland (39%) and Hungary (34%) representing the majority. Fifty-seven (40%) studies had a sample size of less than 100 and there were 20 (14%) studies involving more than 1000 participants. Studies of the two largest populations were a general population sample from Hungary (n=9,407) [80] and a group of chronic obstructive pulmonary disease patients (n=8,537) from Poland [145].
Population norms

There were 14 studies (10%) that involved the general population. These were conducted in Bulgaria (n=1), Hungary (n=4), Poland (n=6) and Slovenia (n=3). Among these, we found representative population norms from Hungary, Poland and Slovenia. Further, local population norms are available for the city of Burgas in Bulgaria.

Clinical areas

Most studies were based on data from patient populations (n=116; 81%). A wide range of clinical areas were covered by the studies, of which diseases of the circulatory system (n=29; 20%), nervous system (n=23; 16%), musculoskeletal system and connective tissue (n=21; 15%), and endocrine, nutritional and metabolic conditions (n=20; 14%) were the most frequent (Figure 3). Hungary led in the number of musculoskeletal (n=13; 29%) and neurologic studies (n=12; 28%), Poland in cardiovascular (n=17; 33%), and nutritional/metabolic studies (n=9; 18%), and the Czech Republic in cardiovascular research (n=7; 39%). There were EQ-5D studies from all eight CEE countries in circulatory diseases. The most common diagnoses were ischaemic heart disease (n=14), diabetes (n=10), Parkinson’s disease (n=9), multiple sclerosis (n=8), chronic pain and rheumatoid arthritis (n=6 for both) (Figure 4). Four studies assessed not only the patients’ health status but the caregivers’ as well.

EQ-5D results: versions of questionnaire, methods of reporting and scores

Eleven studies (8%) employed the EQ-5D-5L. No articles reported results on the youth version of the questionnaire (EQ-5D-Y), possibly because the validation process of the CEE national language versions was only completed in May 2015. There were two studies from Hungary that administered the EQ-5D adult version on paediatric patients aged 6-17, due to the lack of validated Hungarian version of the EQ-5D-Y.
A total of 112 (78%) studies reported EQ VAS scores. We found nine studies that reported only EQ VAS results despite using the descriptive system and five other studies that applied only EQ VAS but not the descriptive system. Further, in four studies only the descriptive system was administered without the EQ VAS.

Out of the 104 (73%) studies that reported responses to the EQ-5D self-classification system, 67 (47%) indicated the percentage of respondents across the five dimensions and 86 (60%) calculated an EQ-5D index score. Almost half of these studies applied the UK tariff (n=41, 48% of 86 studies). Overall 27 (31% of 86 studies) did not specify which tariff was used to calculate the EQ-5D index score. Poland and Slovenia are the only CEE countries with their own national tariff. In Hungary, Bulgaria and Romania, studies were mainly based only the UK value set, in Austria and the Czech Republic on the UK or European, and in Poland and Slovenia on the UK or available national value set.

Total number of EQ-5D index scores reported using the EQ-5D from CEE was 542 and the majority was originated from Hungary (n=248; 46%), Poland (n=104; 19%) and the Czech Republic (n=93; 17%). Mean or median EQ-5D index and EQ VAS scores of studies varied widely and typically patient populations represented the lowest and general population the highest scores in most of the countries (Appendix).

Discussion

The growth and composition of the literature on the EQ-5D in CEE

In this review, we identified 143 published EQ-5D studies in eight CEE countries from the past 15 years. The first publication on EQ-5D from CEE was dated 10 years after the development of the measure. Thereafter, however, has been an increasing trend in the number of published studies from CEE up to 2015 (Figure 2). The growth was the most striking in Hungary and Poland after 2007. For comparison, in August 2015, the EuroQol database contained the following number of studies from other countries: the UK (n=628), Spain (n=234), US (n=230), the Netherlands (n=228), and Germany (n=155) and Canada (n=98). Nonetheless, these are only approximate estimates, because as it is outlined in Figure 1, the records identified for each country in the EuroQol database can differ from the actual number.
of studies meeting the inclusion criteria of this review. One reason for the lag of CEE behind North America, and Northern and Western Europe is that the first EQ-5D studies were published for these countries in the early 1990s, whereas for CEE not until the 2000s. This can be explained by the later introduction of requirements to demonstrate cost-effectiveness evidence for reimbursement decisions [185-187].

**Clinical areas where EQ-5D is used in CEE**

In CEE, cardiovascular (20%), neurologic (16%), musculoskeletal (15%), and nutritional and metabolic diseases (14%) represented the four main fields of research in CEE. Interestingly, in spite of cancer being among the most frequent disease-specific applications of the EQ-5D [29], we found only four oncological studies from CEE: breast cancer [73], lymphoma, leukaemia and myeloma multiplex [70], bone metastases in breast cancer or myeloma multiplex [60] and bladder cancer [14].

After reviewing these 143 papers from CEE, it is unclear why these four clinical areas have become the subject of most EQ-5D studies. The motivation in the background of many studies is not apparent, as 27% of the studies did not include a financial disclosure and 15% were non-funded studies. We assume that a higher-level strategy in topic selection for EQ-5D studies does not exist in CEE countries. Some patterns, however, can be identified that make a bridge between the clinical areas investigated and the funding received. In Hungary, for example, 75% of EQ-5D studies carried out in conditions of the nervous system (including five out of the six Hungarian studies in Parkinson’s disease) were at least partly funded by government organisations. Thus, in Hungary 53% of all governmental sponsorship was directed to the field of neurological research. Similarly, in the Czech Republic, 57% of studies referred to diseases of the circulatory system and received funding from government organisations (50% of all governmental financed studies of the country). It seems therefore that neurological conditions in Hungary and cardiovascular diseases in the Czech Republic were priorities for state-funded EQ-5D research. On the other hand, no similar health policy strategy among projects funded by the EU or the EuroQol Group could be identified. From the latter two sources, mainly data collection for establishing country-specific population norms and various EQ-5D related methodological researches were financed in CEE. Considering all eight countries, the diseases that received the most funding from pharmaceutical or medical device companies and foundations were diabetes including diabetic neuropathy, ischaemic heart disease, multiple sclerosis and osteoporosis.
Only four studies assessed EQ-5D of caregivers; however, having a family member with a chronic illness may impose a substantial burden on the caregiver. In the recent years, the literature concerning this spillover effect has largely evolved, but this QALY loss is typically still not incorporated in cost-effectiveness analyses [188-191].

The distribution of clinical areas covered by the studies in CEE cannot be compared to other countries or regions due to the lack of such data. Between 2009 and 2013, over 6,800 EQ-5D studies have been registered [192]. Nevertheless, no sort order, such as ICD groups or individual diagnoses, is given for the total number of registrations, that hampers to produce a meaningful comparison with our data [192].

**Methodological deficiencies in studies**

Substantial heterogeneity was found in the quality of papers. Methodological deficiencies, such as the lack of reporting either EQ-5D index scores (40%) or EQ VAS scores (22%) and not stating which tariff was used (in the 31% of the studies that calculated EQ-5D index score), were the leading causes of poor quality. Some studies indicated recording only the EQ VAS but not the descriptive system [150,167,158,137,125,159]. In one study, the EQ VAS scale was modified to range from 0 to 10 [173]. Alternative scoring techniques occurred in some studies; for example, the ordinal numeric labels for the health state levels in the instrument (1-3 or 1-5) were treated as cardinal values that can be summed [51,90,95,163,54,116,126,131,65,171,173], which is a flawed concept because these numbers have no intrinsic arithmetic properties. Another study expressed the EQ-5D index score as a percentage [72], which can be misleading when considering the possible negative values. To overcome these methodological shortcomings, the standards outlined in the EQ-5D User Guide should be met [193]. Further, stating the period when the study was conducted (25%) and disclosing the source of financing (27%) were commonly missing in published studies. These are important points to improve methodological quality and the transferability of studies.

Overall, 7% of studies were RCTs (Austria n=2, Hungary n=5, Poland n=2 and Slovakia n=1), which seems low considering the rate of RCTs to total number of EQ-5D studies registered globally between 2009 and 2013 (29% of some 6,800 studies) [192]. This might be partly explained by the fact that, according to the HTA guidelines in CEE countries, patient-reported study data from clinical trials is not necessary for reimbursement submissions [1].
Also, multi-country RCTs, in which no individual results of CEE countries were reported, were excluded from this review.

**Decision-makers' guidance on the approach for estimating utilities in CEE**

In countries such as Poland (n=51) and Hungary (n=47), where the most EQ-5D studies have been carried out within CEE, HTA bodies encourage the use of indirect methods, particularly the EQ-5D, to elicit utilities for economic evaluations in reimbursement applications (Table 1) [24]. In contrast, we have found very few published papers from the other six countries. In most of these countries, there is no preferred choice of instrument to assess utilities with the exception of Slovakia, where direct methods are recommended according to HTA guidelines, and Romania which suggests the EQ-5D based on UK and French recommendations [3,5,8,1]. Apparently, the inclusion of EQ-5D as a preferred instrument in national HTA guidelines plays a key role in promoting the use of EQ-5D.

In all countries studied, pharmaceutical companies are required to submit quality of life data as well as cost-effectiveness or cost-utility analysis, when demanding reimbursement for new drugs (Table 1). Yet it is unclear how these results are used [194-196]. In the near future, given the developments of HTA, the use of health state utility evaluations as an aid to healthcare decision makers will probably sharply increase in CEE. However, to be relevant for health policy decisions, studies must be valid, comparable, reliable, relevant to the policy context and communicated to the appropriate decision makers.

Up unto the end of 2013 more than 2,500 reimbursement decisions have been made in a group of selected CEE countries such as Poland, the Czech Republic, Hungary, Romania and Bulgaria[1]. In contrast the number of EQ-5D studies was merely 75 during this period. Transferring EQ-5D data from other jurisdictions seems to be the major source of the cost/QALY calculations and financing decision-making in CEE [9]. Nevertheless, in HTA guidelines of CEE countries, no guidance is provided as to how (and from which countries) to transfer EQ-5D results. Cost/QALY calculations based on EQ-5D results from other countries might be biased due to various methodological reasons (e.g. differences in tariffs, patient populations, response-scale heterogeneity etc.) [197,198]. Thus, more emphasis should be placed on generating locally-relevant data in the future.
What could/should analysts do in situations where there is no national value set and what are the implications of the various options?

To date, only two CEE countries have their own national value sets: Poland and Slovenia. (Poland is not listed on the website of EuroQol (www.euroqol.org) as their tariff was not produced as a part of the EuroQol Group.) In Austria, the Czech Republic, Poland and Slovenia, different value sets have been used to calculate EQ-5D index scores (despite the fact that Poland and Slovenia have their own national tariffs). This has the drawback that it prevents a proper comparison between results of studies undertaken in the same country. In Hungary, in contrast, the UK value set was applied pragmatically in all studies including the population norm, which has been used as a reference in several studies to assess the utility loss of specific patient populations. Although using other countries’ value sets for economic purposes is acceptable in the absence of local tariffs, it has weaknesses because variations in utility values assigned to the same EQ-5D health states can occur among countries [199-204]. By employing tariffs deriving from the population of another country, utility weights and QALY gains may represent different societal and even cultural values; thus, healthcare resource allocation decisions based on these estimates of QALYs gained may not reflect the societal preferences in the country of interest.

We believe that in those countries, such as Hungary and the Czech Republic, where the number of studies is relatively high and clearly shows an increasing trend, the establishment of country-specific tariffs should be promoted. In practice, however, two major issues would remain unresolved, comparability between earlier and new studies and across countries. If all CEE countries developed their own value sets, the comparisons across the region will become more challenging because of the differences caused by the methodological variations in developing new value sets [197]. Therefore, when a country constructs its own value set (for the 3-level and/or the 5-level versions), we suggest presenting the results thereafter both with the new national and the UK tariffs which has been used as a kind of “common language” up to date to calculate the EQ-5D index score in the region. Results of earlier EQ-5D studies, wherever feasible, could be adapted by applying the new tariff as well. We believe that otherwise the loss of consistency and comparability across CEE countries largely outweighs the gain achieved with the more accurate utility values resulting from the application of different country-specific tariffs. In further studies in CEE countries with no national value set, we recommend the application of the UK tariff, which has been used in the largest number of studies in the region. Further, similarly to the European value set, which was
developed in six countries including Finland, Germany, The Netherlands, Spain, Sweden and the UK [205], a common CEE EQ-5D tariff could be the first step of the collaboration between CEE countries. This would facilitate regional comparisons, and these are assumed to share some characteristics that might drive the health state valuations, a regional tariff would be more appropriate to be used for financial decisions until country-specific value sets are obtained.

Conclusions

Research activity with the EQ-5D is increasing in the CEE region; however, some clinical areas with high health and economic impact are understudied. Considerable variability can be observed between countries both in terms of the proliferation of use and the methodological quality of studies. Our results provide a basis to develop research agenda at the national level as well as for regional collaborations. Other countries may also learn from the experience from this review. First, late adopters, such as CEE, are those that indeed determine the worldwide spread of the EQ-5D. Second, if payers and policymakers in a country are fully committed to cost-effectiveness, they are more likely to take the extra burden of appropriate measurement of health outcomes. Third, as transferring utilities from one country to another remains the major source of utilities, there is a need for some translational guidelines for taking utility estimates and adapting them for local use.
Table 1 Preferred outcomes in the pharmacoeconomic guidelines in CEE countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Preferred analytical technique</th>
<th>Preferred outcome measure</th>
<th>Preferred method to derive utility</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulgaria</td>
<td>CEA/CUA</td>
<td>QoL, QALY</td>
<td>Quality of life measures (not specified)</td>
<td>Methodological guideline for presentation of documents for evaluation of the efficacy, safety and pharmacoeconomic indicators of medicinal products for application for inclusion into the Positive Drug List (2015) [22]</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>not recommended</td>
<td>QoL, QALY</td>
<td>Disease-specific or generic questionnaires</td>
<td>Czech Pharmacoeconomic Society (2009) [8]</td>
</tr>
<tr>
<td>Hungary</td>
<td>CMA, CEA, CUA</td>
<td>QoL, QALY</td>
<td>Using a preference-based multidimensional health related quality of life questionnaire (EQ-5D, Health Utilities Index, a Quality of Well-Being Scale or Years of Healthy Life) is recommended in the first place.</td>
<td>Ministry of Human Resources, Hungary: Technical Guideline for the Making of Health-Economic Analyses (2013) [2]</td>
</tr>
<tr>
<td>Poland</td>
<td>CEA, CUA, CCA</td>
<td>QoL, QALY</td>
<td>The preference measurement for the purposes of utility assessment is possible by using direct or indirect preference measuring methods. It is recommended to use indirect methods for preference measurement – validated questionnaires in Polish. While measuring preferences with the EQ-5D questionnaire, it is advised to use the Polish utility standard set obtained by means of the TTO method.</td>
<td>Agency for Health Technology Assessment. Guidelines for conducting Health Technology Assessment (HTA). Version 2.1. Warsaw (2009) [4]</td>
</tr>
<tr>
<td>Romania</td>
<td>CEA/CUA</td>
<td>QALY</td>
<td>Having benchmarking NICE/SMC/AWMSG recommendations report EQ-5D can be considered preferred</td>
<td>Gulácsi et al. 2014 [1]</td>
</tr>
<tr>
<td>Slovakia</td>
<td>CUA if the treatment has an impact on health-related QoL that is significant to the patient or if there are multiple patient-relevant clinical outcome parameters</td>
<td>QoL, QALY</td>
<td>TTO or SG (VAS)</td>
<td>Ministry of Health, Slovakia (2008) [3]</td>
</tr>
<tr>
<td>Country</td>
<td>Methodology</td>
<td>Outcomes</td>
<td>Instrument</td>
<td>Source</td>
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<tr>
<td>Slovenia</td>
<td>CEA/CUA/CMA/CA</td>
<td>QALY (intermediate outcomes can be accepted, such as blood pressure, cholesterol, glycosylated hemoglobin, and hospitalization)</td>
<td>There is no preferred instrument.</td>
<td>Assembly of the Health Insurance Institute (2010)</td>
</tr>
</tbody>
</table>

AWMSG = All Wales Medicines Strategy Group, CA = cost analysis, CCA = cost consequences analysis, CEA = cost-effectiveness analysis, CMA = cost minimisation analysis, CUA = cost-utility analysis, NICE = National Institute for Health and Care Excellence, QoL = quality of life, QALY = quality adjusted life year, SMC = Scottish Medicines Consortium, SG = standard gamble, TTO = time trade-off, VAS = visual analogue scale.
## Table 2 Characteristics of the studies

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<thead>
<tr>
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<td>27%</td>
</tr>
</tbody>
</table>

ICD-10 = International Statistical Classification of Diseases and Related Health Problems 10th Revision; N/A = not applicable; NR = not reported; RCT = randomised controlled trial
* One study may refer to more than one subgroup within the following categories: study sample, methods of data collection, tariffs used and funding source.
§ Percentage indicates the rate to the total number of studies that estimated EQ-5D utility score (n=86).
§§ All studies from Bulgaria, Hungary and Romania employed the UK tariff but in some studies other tariffs were as well applied together with the UK one.
Figure legends

Figure 1 PRISMA flowchart of the study selection
Searched: July 1, 2015.
* Literature search was conducted on a country basis; thus, the total number of studies is slightly higher than the real number of studies.
** Total number of studies in this row is not equal to the sum of the ‘country columns’, because one study included 6 and another 5 CEE countries [45,46].

Figure 2 Number of EQ-5D studies published in CEE countries from 2000 onwards
CEE – Central and Eastern Europe

Figure 3 ICD-10 classification of the studies
One study may refer to more than one ICD-10 group. The sum of percentages is less than 100% as the percentages indicate the proportion of a given ICD-10 group out of the total number of studies including population-based studies.

Figure 4 Most common diagnoses/clinical areas among the studies
The size of bubbles refer to the total number of patients of studies in a given diagnosis/disease group (i.e. the numbers in brackets after diagnoses). For studies that assessed EQ-5D in various patients groups, only the number of patients with the diagnosis/or clinical area of interest is included in this figure.
COPD = chronic obstructive pulmonary disease; PAOD = peripheral arterial occlusive disease
## Appendix - Lowest mean EQ-5D index and EQ VAS scores by country

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<td>Poland</td>
<td>-0.03</td>
<td>stroke, Modified Rankin Scale 5</td>
<td>[160]</td>
<td>22.50</td>
<td>low back pain or sciatic nerve pain</td>
<td>[125]</td>
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<tr>
<td>Romania</td>
<td>0.75</td>
<td>coronary heart disease</td>
<td>[45]</td>
<td>59.15</td>
<td>coronary heart disease</td>
<td>[46]</td>
</tr>
<tr>
<td>Slovakia</td>
<td>0.52</td>
<td>degenerative lumbar spine preoperatively</td>
<td>[166]</td>
<td>51.00</td>
<td>critical limb ischaemia</td>
<td>[167]</td>
</tr>
<tr>
<td>Slovenia</td>
<td>0.54</td>
<td>multiple sclerosis</td>
<td>[176]</td>
<td>49.20</td>
<td>multiple sclerosis</td>
<td>[176]</td>
</tr>
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References


10. The Act on Reimbursement of Medicines, Foodstuffs Intended for Particular Nutritional Purposes and Medical Devices from 12th of May, 2011 (Journal of Laws, No. 122, item 696)


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