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INTERNATIONAL REGULATIONS AND RECOMMENDATIONS FOR UTILITY DATA FOR HEALTH TECHNOLOGY ASSESSMENT

Running title: INTERNATIONAL REGULATIONS AND RECOMMENDATIONS FOR UTILITY DATA FOR HEALTH TECHNOLOGY ASSESSMENT

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Abstract

Recommendations and guidelines for the collection, generation, source and usage of utility data for Health Technology Assessment (HTA) vary across different countries, with no international consensus. Many international agencies generate their own guidelines providing details on their preferred methods for HTA submissions, and there is variability in both what they recommend and the clarity and amount of detail provided in their guidelines. This article provides an overview of international regulations and recommendations for utility data in HTA for a selection of key HTA countries: Australia, Canada, France, Germany, The Netherlands, Spain (Catalonia), Sweden and UK (England and Wales, Scotland).

The article finds that international guidelines are typically clear and detailed for the selection of countries assessed regarding the source description of health states (for example generic preference-based measure) and who should provide preference-weights for these health states (for example general population for own country). Many guidelines specify the use of off-the-shelf generic preference-based measures, and some further specify a measure, such as EQ-5D. However international guidelines are either unclear or lack detailed guidance regarding the collection (for example patients report own health), source (for example clinical trial) and usage (for example adjusting for comorbidities) of utility values.

It is argued that there is a need for transparent and detailed international guidelines on utility data recommendations to provide the best possible evidence to decision-makers. Where this is not possible it is recommended that best practice should be used to inform the collection, source and usage of utility values in HTA.

KEY POINTS FOR DECISION MAKERS

- There is no international consensus on guidelines for the collection, generation, source and usage of utility data for health technology assessment.
- Individual country recommendations regarding the generation of utility data are typically clear and detailed for the key countries assessed regarding a) the source description of health states e.g. generic preference-based measure and b) who should provide utility values for these health states e.g. general population for own country.
- Individual country recommendations are unclear or not stated regarding a) who should complete the questionnaire, b) the source e.g. clinical effectiveness trial and c) methodological options when using utility data in the economic model e.g. adjusting the baseline for age.

1. Introduction

There is no international consensus on guidelines for the use of utility data for health technology assessment (HTA) and many international agencies generate their own guidelines providing details on their preferred methods for HTA submissions. This has implications for research and trial design. This paper provides an overview on international HTA guidelines for key HTA countries (n = 9) pre-selected as representative settings by the authors: Australia (Pharmaceutical Benefits Advisory Committee (PBAC) [1]), Canada (Canadian Agency for Drugs and Technologies in Health (CADTH) [2]), France (Haute Autorité de Santé (HAS) [3]), Germany (German National Institute for Quality and Efficiency in Health Care (IQWiG) [4]), The Netherlands (College voor zorgverzekeringen (CVZ) [5]; Busschbach et al[6]), Spain (Catalonia) (CatSalut [7]), Sweden (Pharmaceutical Benefits Board [8]), and the United Kingdom (UK) for England and Wales (National Institute of Health and Care Excellence (NICE) [9]) and Scotland (Scottish Medicines Consortium (SMC) [10]). This list is not exhaustive and does not reflect all international guidance, in particular it focuses upon Western Europe, Australia and Canada, and does not include guidance for Africa, Asia, Latin America and Eastern Europe. Furthermore this does not include guidance from groups such as the Washington Panel [11] or ISPOR [12] which produce comprehensive guidance on best practice for HTA. This paper summarises these guidelines for the collection, generation, source and usage of utility data for HTA submissions, and provides definitions of the concepts involved. Additional detailed information included in the guidelines are provided in the accompanying online supplementary material.

An important point of clarification is that issues can either be 'not stated', 'recommended' or 'required'. Not stated means that there is no guidance explicit in the methods guidelines for a given country. Recommended or preferred suggests that the agency in the country would prefer the method, but it is implicit that they are open to considering alternative methods if appropriately justified, though how open they are may depend on the exact issue and agency. Required states a strong preference where the agency may reject HTA submissions not meeting the requirements, and this means that there are few requirements specified within the guidelines.

1 Summary of international recommendations for economic evaluation for a selection of countries

Table 1 provides a summary of the economic evaluation methods that are recommended by each of the international guidelines.

1.1 Cost-utility analysis

For all guidelines cost-utility analysis, where effectiveness is measured using quality adjusted life years (QALYs), is the preferred form of economic evaluation with the exception of Germany.

1.2 Perspective

Guidelines for Canada, Germany, Scotland, Spain, and England and Wales recommend a health service perspective which includes costs incurred by the health service in the economic evaluation. Guidelines for France, The Netherlands and Sweden recommend a societal perspective which includes wider societal costs in addition to costs incurred by the health service in the economic evaluation, for example productivity costs, or informal care costs, costs incurred by patient and or carer/family (the exact inclusions can vary by country). Whilst Australian guidelines recommend a societal perspective in the guidelines it is extremely rare that Australian submissions take this perspective. The choice of perspective is important, as this determines which costs and benefits can be included in the economic evaluation, and this can impact on the cost-effectiveness results.

1.3 QALY weighting

The standard approach is to assume that a QALY gained is of equal value regardless of who gains that QALY, meaning that all QALYs are given the same QALY weight of 1. With the exception of the Netherlands 2015 guidance only available in Dutch (see [13] for further details in English on the Netherlands guidance), all guidelines recommend equal QALY weighting, either explicitly or implicitly through not specifying any QALY weighting considerations. This means that a QALY is given a weighting of 1 and is of equal worth for every recipient, regardless of their characteristics such as age, for example age 10 or 80.

However, an alternative approach is to use QALY weighting where a higher (or lower) weight is given to QALYs gained by certain patients, for example those who are at the end of their life. The Netherlands 2015 guidance refers to different thresholds depending on the necessity of the intervention. Australian guidelines state that equity issues can be outlined where these are important and relevant. England and Wales guidelines state that a higher QALY weight may be given for life-extending treatments provided to patients at the end of their life where life expectancy is short (normally less than 24 months), treatment offers an additional 3 or more months and the target population is small. The HSUVs themselves remain unaltered, but in effect face a different threshold which can mean they are funded although they would not be considered cost effective using the standard guidelines. For example, in England and Wales guidelines cancer treatments for

end of life patients or orphan drugs may be funded despite having a cost-per-QALY value greater than the standard cost-effectiveness threshold used.

1.4 Carer utility values

Carer utility values reflect the health-related quality of life of the carer (rather than the patient). These can be considered important for economic evaluation of diseases with large carer input and where the intervention can impact on the health-related quality of life of the carer. Guidelines for Canada, Germany, Scotland and the Netherlands 2015 guidelines state that carer utility values (i.e. the utility of the carer of the recipient of the intervention), can be included if relevant, although this is typically to be considered separately rather than in the base case analysis (**Table 1**). England and Wales guidelines state that carers' utility values should be included in the base case when relevant. The remaining guidelines do not refer to carers' utilities. Carer measures include the CarerQol [14,15] and the Carer Experience Scale [16] though neither are anchored on the 1-0 full health to dead scale required for QALYs.

Table 1 International recommendations for economic evaluation

Country	Producing Body	Year	CUA is preferred form of economic evaluation	Recommended perspective	Equity considerations for QALY weighting	Carer utility values
Australia	PBAC [1]	2013	Yes	Societal (though uses non-standard definition)	Equal QALY weighting. Equity issues outlined where important and relevant	Not mentioned
Canada	CADTH [2]	2006	Yes	Publicly funded health care system	Equal QALY weighting	If relevant report separately
France	HAS [3]	2012	Yes	Societal	Equal QALY weighting	Not mentioned
Germany	IQWiG [4]	2015	No	Health care. Optional perspectives are social insurance and societal	Not mentioned	If relevant carer consequences can be considered
The Netherlands	CVZ [5,6]	2006	Yes	Societal	Different thresholds depending on the necessity of the intervention in 2015 guidance in Dutch	Not mentioned
Spain (Catalonia)	CatSalut [7]	2014	Yes	Catalan Health Service. Societal may be provided separately	Equal QALY weighting	Not mentioned

Country	Producing Body	Year	CUA is preferred form of economic evaluation	Recommended perspective	Equity considerations for QALY weighting	Carer utility values
Sweden	Pharmaceutical Benefits Board [8]	2003	Yes or CEA	Societal	Not mentioned	Not mentioned
UK: England and Wales	NICE [9]	2013	Yes	NHS and PSS	Equal QALY weighting. QALY weighting acceptable for life-extending treatment at end of life for patients with short life expectancy and small patient populations	All direct health effects should be included for patients or, when relevant, carers
UK: Scotland	SMC [10]	2016	Yes	NHS in Scotland and social work	Equal QALY weighting	Not included in reference case, if relevant report separately

Key: CADTH – Canadian Agency for Drugs and Technologies in Health; CEA – cost effectiveness analysis; CUA – Cost utility analysis; CVZ - College voor zorgverzekeringen; HAS – Haute Autorité de Santé; IQWiG - German national institute for quality and efficiency in health care; NHS – National Health Service; NICE – National Institute for Health and Care Excellence; PBAC - Pharmaceutical Benefits Advisory Committee; PSS – Personal Social Services; SMC – Scottish Medicines Consortium.

2 Overview of international recommendations for utility data

Table 2 provides a summary of the alternative methods that are recommended by each of the international guidelines to produce health state utility values (HSUVs), as these form the 'Q' quality adjustment weight of the QALY, i.e. the utility values anchored on the 1-0 full health-dead QALY scale required to generate QALYs.

2.1 Preferred method for generating HSUVs

2.1.1 Generic preference-based measures

A generic preference-based measure (generic PBM) is an 'off the shelf' measure which classifies each patient to a health state which has a corresponding utility value obtained from an existing set of preference weights typically obtained from a representative sample of the general population. Most guidelines included in the review recommend the use of an existing PBM to generate HSUVs, and some further specify a measure, for example Scotland and England and Wales recommend EQ-5D, the Netherlands recommend EQ-5D-5L and Spain (Catalonia) recommend either EQ-5D or SF-6D. The main advantage of using the same standardized PBM for all HTA submissions for a particular country is that it enables comparability across all interventions, providing consistency in the resource allocation process. In addition their performance across a wide range of conditions is well established and psychometric properties well known [17].

2.1.2 Condition-specific preference-based measures

A condition-specific preference-based measure (CSPBM) is a measure of health-related quality of life that is specific to a certain condition or disease and that also has an off-the-shelf set of preference weights that enables HSUVs to be generated from responses to the measure. None of the guidelines recommended condition-specific preference-based measures as the preferred method for generating HSUVs. This is most likely because they do not enable comparability across different interventions in different conditions, presenting a challenge for consistency in resource allocation decisions across all interventions and conditions [18].

2.1.3 Vignettes

Vignettes (also referred to as scenario-based utility valuations) are bespoke descriptions of a small number of health states specific to the states used in the economic model, typically the descriptions of health states are generated by interviews with clinicians or patients [18]. Only Australian guidelines state that they accept HSUVs elicited using vignettes to provide the health state description (though this is not their preferred technique and it is expected that the values would be

scrutinised). One advantage of vignettes is that they can be tailored to suit the economic model and can be flexible in terms of what is included in their description. However, vignettes are not regarded favourably by the international agencies as they are not comparable across different interventions or patient groups. Furthermore they do not reflect the variability of outcomes experienced by patients in clinical trials [19]. In addition their construction can be subjective and hence they can be prone to inaccurate valuations due to focussing effects as respondents valuing the health states are likely to focus on what exactly is described in the health state, yet what is described in the state may not be an accurate description.

2.1.4 Direct utility elicitation

Direct utility elicitation is where patients are asked to directly value their own health using an elicitation technique such as standard gamble or time trade-off (see [20] for an illustration of the use of direct utility elicitation to value the EQ-5D in Sweden). Direct utility elicitation is recommended in the Swedish guidelines to produce HSUVs. The advantage of direct utility elicitation is that the values do not rely upon the accuracy of the described health state as respondents will value their own health rather than a description of their own health. There are ethical concerns with asking patients to value their own health when they have to consider whether they would rather die than live in their current state, which is required in the standard gamble and time trade-off elicitation techniques that enable values to be anchored onto the 1-0 full health-dead scale required to generate QALY values. In addition patients may have adapted to their poor health and may have adjusted their expectations and understanding of what it is like to live in full health, and this can impact on the values they provide (potentially providing higher values than the general population though we are not aware of any literature providing direct utility values that represent the range of possible health states). There are also concerns about the representativeness of patients providing direct utility values, as those in very poor health or who are very dissatisfied with their health may not provide values [21].

2.2 Elicitation of preference weights

A preference weight is a numerical judgement of the desirability of a particular outcome or situation. There is a choice of whose values should be used to generate preference weights, and which technique should be used to elicit the values (see [17] for an overview).

2.2.1 Preferred population used to elicit preference weights

Preference weights for PBMs (or vignettes) can be elicited from the general population, patients, or clinicians/experts, where samples of people state how good and bad they think different health states are using an elicitation method (see below). Most international agencies (Australia, Canada, France, The Netherlands, Spain, England and Wales, Scotland) prefer that the general population is used to provide preference weights rather than patients or clinicians/experts. Using preference weights elicited from the general population has the advantage that the general population typically fund health care via taxation, and they have no vested interest as they do not know which conditions they will have in the future. However, they may not take into account adaptation, where patients adapt to their condition over time, and may instead provide values that represent what it is initially like to be in a poor state which can lead to a lower utility value than is fully representative of all patients living in that state. Out of the guidelines included in the review only Sweden and Germany recommend that patients are used to elicit preference weights. However, there are concerns with the use of preference weights elicited from patients, as (as also outlined above for direct utility elicitation) patients may have adapted to their poor health and may have also adjusted their expectations and potentially their understanding of what it is like to live in full health, and this can impact on the HSUVs they provide.

Guidelines for Australia, France, Germany, The Netherlands, Spain, and England and Wales recommend that members of their own country are used to provide preference weights, i.e. the value set used to provide the preference weights for the health states must be derived using a sample from their own country. For Germany this involves a sample of patients, but for Australia, France, the Netherlands, Spain and England and Wales this involves a sample of the general population. The recommendation of using own country values is based on evidence that shows that value sets differ across different countries, as different populations have different cultures, social fabric, family structure, working habits and so forth and this can all impact on the weight given to the individual health state. In addition languages differ and this can impact on values, for example being “depressed” (English) and being “depressief” (Dutch) may have different emotional interpretations. Therefore to ensure that the HSUVs used in an economic evaluation represent the country population of interest, it is advisable to use the country specific preference weights, i.e. the preference-based value set where available.

2.2.2 Preferred elicitation method

Preference elicitation methods are used to elicit HSUVs for different health states, and methods include standard gamble, time trade-off or VAS (visual analogue scale). Preference elicitation

methods could be used to value a preference-based measure such as the EQ-5D or a CSPBM, to value vignettes, to value health states in a model, or to value the patients' own health i.e. direct utility elicitation. Standard gamble (SG) is a technique where respondents choose between two options: a) an impaired health state for certain, and b) a gamble where there is a probability of being in full health and a probability of immediate death. The probability of full health is varied until the respondent is indifferent between the two options, and the utility value of the impaired health state is the probability of full health. Time trade-off (TTO) is a technique where respondents choose between an impaired health state for, say, 10 years and full health for x years where x≤10. Each state is followed by immediate death. The number of years in full health is varied until the respondent is indifferent between the two options, and the utility value of the impaired health state is the number of years in full health. VAS is a technique where a respondent records a mark for an impaired health state on, say, a line numbered from 100-0, best health imaginable-worst health imaginable, and this mark is the value of the impaired health state. To obtain a value on the 1-0 full health-dead scale required for QALYs a mark also needs to be recorded for dead and the value of the impaired health state rescaled accordingly.

All guidelines recommend the use of SG or TTO to elicit utility weights (with the exception of Germany which does not recommend the inclusion of HSUVs in economic evaluation), and Sweden also recommend the use of visual analogue scale VAS. Guidelines for Scotland, Spain and England and Wales specify only that the method should be choice-based, which is essentially SG or TTO as these are the most common choice-based methods. Typically choice-based methods are recommended because they incorporate a notion of sacrifice, where respondents make a sacrifice to obtain their choice, and it has been argued that this obtains stated preferences that are more representative of actual preferences. For example, in the time trade-off task respondents choose whether to sacrifice years of life for better health-related quality of life. This is in contrast to VAS where respondents place the health state on a numerical scale, and there is no sacrifice involved. Other methods used to generate utility values such as ranking, discrete choice experiment and best-worst scaling are not recommended in any of the guidelines, though discrete choice experiment is referred to in the guidelines for Australia and the Netherlands.

2.3 Who should complete the questionnaire used to generate HSUVs

All guidelines either implicitly or explicitly recommend that patients report their own health-related quality of life, i.e. complete the questionnaire used to generate HSUVs, reflecting the belief that it is people in the condition themselves who have better knowledge and understanding of their own

levels of health functioning and symptoms on a daily basis. If patients are unable to report their own health-related quality of life, for example due to their level of cognitive functioning, some guidelines (France, Spain, England and Wales) explicitly recommend that a proxy may do this on their behalf. This proxy could be a family member/primary carer or friend, or more rarely a health care professional.

Table 2 International recommendations for measuring and valuing HRQoL

Country	Preferred method for generating HSUVs	Alternative to preferred technique	Direct utility assessment accepted	Preferred population used to value health states	Preferred elicitation method	Patients should report own HRQOL
Australia	Generic PBM: HUI2, HUI3, EQ-5D, SF-6D, AQoL	Direct utility assessment, vignettes (referred to as scenario-based utility valuation), mapping, utilities from the literature	Yes	Australian general population	SG or TTO	Yes (implicit)
Canada	PBM (encouraged, implicit this is a generic PBM) or direct utility assessment	Willingness to pay	Yes	General population	SG or TTO	Yes (implicit)
France	EQ-5D or HUI3 or any other PBM with validated French preference weights	CSPBMs and direct valuations of descriptions of health states based on a generic questionnaire validated for France	Not mentioned	French general population	SG or TTO	Yes, if inappropriate by proxy
Germany	None (note QALYs are not the preferred technique)	N/A	Not mentioned	German patients	None	Not mentioned
The Netherlands	EQ-5D-5L	(1) The EQ-5D-3L, (2) Other QALY questionnaires such as the SF-6D and the HUI, (3) Domain-specific PROMs, such as FACT-L and EORTC QLQ-C30, (4) CSPBMs, (5) Mapping, (6) The direct valuation of health states in the model, (7) Using quality of life weights from the literature	Not mentioned	Dutch general population	SG or TTO	Yes

Country	Preferred method for generating HSUVs	Alternative to preferred technique	Direct utility assessment accepted	Preferred population used to value health states	Preferred elicitation method	Patients should report own HRQOL
Spain	EQ-5D and SF-6D (from SF-36)	(1) Other generic PBM validated in Spain with Spanish weights e.g. HUI3, (2) generic PBM not validated in Spain with Spanish weights obtained using SG or TTO in general population, (3) EQ-5D and SF-6D data from other countries using Spanish weights, (4) generic PBM data from other countries using non-Spanish weights, (5) mapping to generic PBM, preferably EQ-5D or SF-6D	Not mentioned	Spanish general population	Choice-based method such as SG or TTO	Yes, if unfeasible by proxy
Sweden	Direct utility assessment	PBMs such as EQ-5D	Yes	Patients	SG or TTO preferred. VAS also accepted	Yes (implicit)
UK: England and Wales	EQ-5D	Obtaining utilities from the literature, mapping, other measures	No	UK general population	Choice-based method	Yes or by proxy
UK: Scotland	EQ-5D	Mapped values, direct utility assessment using TTO or SG, utilities from the literature	Yes	General population	Choice-based method such as SG or TTO	Yes

Notes: AQoL – Assessment of Quality of Life; CSPBM – condition-specific preference-based measure; HSUVs – health state utility values; HUI – Health Utilities Index; European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; FACT-L – Functional Assessment of

Cancer Therapy-Lung; PBM – preference-based measure; PROM – Patient-reported outcome measure; SG – standard gamble; TTO – time trade-off; VAS – visual analogue scale.

3 Overview of international recommendations for data source for obtaining utility data for a selection of countries

Table 3 provides a summary of recommended data sources for HSUVs for each of the international guidelines. HSUV evidence for decision analytic models can be sourced from datasets including clinical trials, observational studies and the published literature. The guidelines differ in how explicit and how detailed the recommendations are regarding the accepted sources of evidence for HSUVs. Guidelines for Canada, Sweden and The Netherlands offer little explicit guidance.

3.1 Preferred source for obtaining utility data

Guidelines for Canada, Spain and the Netherlands do not explicitly state a preferred method for retrieving utility data. As discussed above Sweden recommend that HSUVs are direct utility values obtained from patients, and this means that existing studies that involved direct utility elicitation may be important for providing this information.

Some agencies (Australia, Germany, England and Wales, and Scotland) recommend that HSUVs are sourced from clinical trials. However no guidelines explicitly state whether the clinical trial used to source utility data is the same trial that should be used to establish clinical effectiveness of the treatment, and this is an important issue where more explicit guidelines would be useful. It would also be useful to provide a general hierarchy of sources of evidence (such as clinical trial is preferred to literature review) and the circumstances under which different sources of evidence are appropriate, because the quality of methods used within any given source of evidence can impact upon the quality of the evidence.

3.2 Does utility data need to be obtained from own country?

Guidelines for France state that they prefer utility data (i.e. self-reported health from patients scored using an existing value set) obtained from people in their own country (e.g. classification data completed in a French sample and scored using French preference weights). This means that HSUVs used for the health states in the economic model are obtained from own country data. Own country utility data can be provided by using only the data from the own country from a multi-national study. All other guidelines do not explicitly recommend this.

3.3 Mapping

Mapping is a technique that can be used to estimate HSUVs required or 'target' HSUVs where they are not available in a dataset of interest. Mapping can also be used to model existing data to

extrapolate target HSUVs for important clinical end points, and to control for sociodemographic variables important for the decision model. Recently published guidelines include guidance regarding whether mapping is considered acceptable to estimate HSUVs. Guidelines for Australia, Canada, The Netherlands, Scotland and England and Wales state that mapping is acceptable; whereas guidelines for France and Germany state that mapping is unacceptable. All countries where mapping is acceptable provide further guidance around the use of mapped values, such as when it is appropriate or inappropriate (for example in England and Wales it is acceptable to map to EQ-5D if EQ-5D data is not available) and the reporting of the generation of mapped values (for example England and Wales state that the statistical properties should be fully described, the choice of model justified, it should be adequately demonstrated how well the mapping function fits the data and sensitivity analyses should be conducted) [22].

Table 3 International recommendations for sources of HSUVs evidence

Country	Preferred source for obtaining utility data	Can utility data be obtained from clinical trials?	Can utility data be obtained from observational studies?	Can utility data be obtained from the literature?	Should utility data be obtained from own country?[#]	Is mapping an acceptable method to estimate HSUVs?
Australia	Clinical trial	Yes	Not mentioned	Yes (systematic search)	No	Yes
Canada	Not explicit	Not explicit	Yes	Yes	Not mentioned	Yes
France	French data preferred	Not explicit	Not mentioned	Yes	Yes	No
Germany	Clinical study (note QALYs are not the preferred technique)	Yes	Not mentioned	Not mentioned	Not mentioned	No
The Netherlands	Not explicit, implicitly is empirical clinical study	Yes	Yes	Yes	No	Yes
Spain	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Sweden	Direct utility values are preferred, meaning that the use of data from previous studies may be the way of meeting this criteria	Not mentioned	Yes (implicit)	Yes	Not mentioned	Not mentioned
UK: England and Wales	Clinical trials	Yes	Yes	Yes (systematic review)	Not mentioned	Yes
UK: Scotland	Randomised controlled studies of the treatment	Yes	Yes	Yes (systematic review)	Not mentioned	Yes

[#] Note: this is about obtaining utility data (e.g. health self-reported by people with the condition and scored using existing value sets) not about the preference weights for scoring the utility data

4 Overview of international recommendations for use of utility data in the economic model for a selection of countries

The review extracted information on: discount rates for health benefits, baseline or counterfactual HSUVs, adjusting/combining HSUVs (e.g. age, gender, comorbidities, etc.), accounting for treatment-related adverse events, and exploring uncertainty. All guidelines state preferred discount rates varying from 3%-5% in the base case and typically 0% and 5% in sensitivity analyses. However, with the exception of capturing uncertainty, they provide few recommendations or guidance relating to the other items relating to the use of utility data in the economic model. While this is not entirely unexpected, as they are not technical documents, these factors may have a substantial effect on the incremental cost-effectiveness ratio (ICER) [23,24].

All guidelines state that uncertainty should be considered for example using sensitivity analyses, but this is regarding uncertainty in general and the recommendations are not specific to HSUVs. The one exception is the guideline for England and Wales which specifically mentions that when HSUVs are obtained via mapping variance covariance matrices should be reported and these should be incorporated in probabilistic sensitivity analyses.

5 Conclusions and recommendations

Whilst there are similarities amongst the guidelines included in the review, there is no international consensus on guidelines for the collection, generation, source and usage of utility data for health technology assessment. International guidelines regarding the generation of utility data are typically clear and detailed for the selection of countries assessed regarding the source description of health states (for example generic preference-based measure) and who should provide preference-weights for these health states (for example general population for own country). Many guidelines specify the use of off-the-shelf generic preference-based measures, and some further specify a measure, such as the EQ-5D. International guidelines are either unclear or lack detailed guidance regarding the collection (for example patient report own health), source (for example clinical trial) and usage (for example adjusting for comorbidities) of HSUVs. This creates uncertainty for pharmaceutical companies and researchers in trial design, in the sourcing of HSUVs and the construction of economic models.

Whilst there are many aspects where countries may legitimately have different preferences, for example on their preferred elicitation technique, there are aspects where best practice can be defined to inform guidelines. There is a need for transparent and detailed international guidelines on

utility data recommendations to provide the best possible evidence to decision-makers. Where this is not possible it is recommended that best practice should be used to inform the collection, source and usage of HSUVs in economic models, as outlined in the remaining chapters [25,26,27,22,28,23,24].

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Author contributions

DR extracted and analysed the evidence from the literature, wrote the first draft of the manuscript and made final edits. IA extracted some data, checked the extraction and contributed to the manuscript. HC contributed to the manuscript. BvH checked the extraction and contributed to the manuscript.

Compliance with Ethical Standards

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