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**Title:** Estimation of societal values of health states preferences at the national level for low- and middle-income countries (LMICs).

**Authors:** Oscar Espinosa, M.Sc., MBA.1, Michael Drummond, Ph.D.2, Luis-Esteban Orozco, M.Sc.3, Angélica Ordoñez, M.Sc.4, Daysi Sanmartín, M.Sc.3, Laura Mora, M.Sc.5, Jessica Ochalek, Ph.D.2.

1. Economic Models and Quantitative Methods Research Group (IMEMC), Centro de Investigaciones para el Desarrollo, Universidad Nacional de Colombia, Colombia, Bogotá, D.C.

2. Centre for Health Economics, University of York, United Kingdom, York.

3. School of Economics, Universidad de Antioquia, Colombia, Medellín.

4. Directorate of Analytical, Economic and Actuarial Studies in Health, Instituto de Evaluación Tecnológica en Salud (IETS), Colombia, Medellín.

5. Department of Health Services Research and Policy, Faculty of Public Health and Policy, London School of Hygiene & Tropical Medicine, United Kingdom, London.

**Corresponding author information:**

Oscar Espinosa, M.Sc., MBA.

Director Economic Models and Quantitative Methods Research Group (IMEMC), Centro de Investigaciones para el Desarrollo, Universidad Nacional de Colombia.

Colombia, Bogotá D.C., Carrera 30 N°. 45–03, 111321.

Email: oaespinosaa@unal.edu.co

Phone: +57 3134636126.

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*Acquisition of data*: Espinosa, Orozco, Ordóñez, Sanmartín, Mora.

*Analysis and interpretation of data*: Espinosa, Orozco, Ordóñez, Sanmartín, Mora.

*Drafting of the manuscript*: Espinosa, Drummond, Orozco, Ordóñez, Sanmartín, Mora, Ochalek.

*Critical revision of the paper for important intellectual content*: Espinosa, Drummond, Orozco, Ordóñez, Sanmartín, Mora, Ochalek.

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**Highlights**

* Historically, there has never been, and perhaps never will be, a complete consensus on the strategies to measure the preferences for health states. However, their application may play a fundamental role in conducting clinical trials, as well as in decision-making in public policy decisions on health (local, regional, and national levels).
* Among the main findings of this study is that only 19 LMICs classified by the World Bank have estimated nationally representative societal values of health states preferences. The most frequently applied generic instrument to measure health-related quality of life was the EQ-5D-5L and the EQ-5D-3L, with face-to-face interviews being the most common form of administration.
* The statistical methods most frequently used to study health-related quality of life values were ordinary least squares, generalised least squares, Tobit, and logit, as well as hybrid approaches. In contrast, the Bayesian approach was only present in two studies.

**Title:** Estimation of societal values of health states preferences at the national level for low- and middle-income countries (LMICs)

**Abstract**

**Background:** Social preference values of health states are a fundamental input for the preparation of studies in health economics. Several countries have taken undertaken studies to obtain these values. Our objective was to conduct a structured and systematic literature review that calculates this set of representative values at the national level in low- and middle-income countries (LMICs).

**Methods:** In this systematic review,we searched the Embase, MEDLINE, Ovid, SciELO, and LILACS databases, among others, for studies published up to June 2022, that estimated nationally representative health states preferences values for LMICs. We summarised the information qualitatively and assessed the risk of bias in each paper using the COSMIN checklist tool.

**Results:** Of the 23663 articles identified, 35 studies were eligible for inclusion. The studies were from 19 countries in Latin-American, Europe, Africa, and Asia. No studies were found for low-income countries. The most commonly applied generic instrument for measuring health-related quality of life was the EQ-5D-5L and EQ-5D-3L. Preference was given to face-to-face administration of these instruments. The sociodemographic variables with the most significant negative correlation versus utility were older adults, marital status (widowed or divorced), and low educational level and income.

**Conclusions:** Worldwide, there have been few studies that have estimated, in a nationally representative manner, the social values of health states preferences in LMICs. We consider the local estimate of this set of societal values relevant for any society to improve decision-making in allocating resources in health budgets.

1. **Introduction**

Health Technology Assessment (HTA) is currently defined as a *“multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle”* 1. As one of its main objectives is to inform decision-making that promotes the quality, equity, and efficiency of health spending in a context of finite resources, health economic evaluation (HEE) stands out as a fundamental component of HTA. HEE is understood as the comparative analysis between costs and health outcomes of alternative health technologies 2 and comprises five critical types of analysis: cost-effectiveness, cost-benefit, cost-minimization, cost-consequence, and cost-utility analysis.

This last type of analysis is frequently used, and measures health outcomes with generic quality and life expectancy measures, which require country-specific valuations of health states 3,4. Thus, it is necessary to estimate health states preferences values (utilities) to determine the health benefit of providing or funding a health technology (which may be a diagnostic tool, a pharmaceutical drug or a program of care). Cost-utility analysis (CUA) calculates an incremental cost-effectiveness ratio of providing or funding the technology as the differences in costs and differences in health outcomes, such as quality-adjusted life years (QALYs), disability-adjusted life years (DALYs), or any other assessment based on health states preferences 5–8, between a technology and its next best alternative. This enables decision-making to be informed in a manner that promotes a financially sustainable, equitable, efficient, and high-quality health system 2. However, there are limitations, in that quality of life measures can be more subjective than clinical indicators, and that the CUA fails to capture impacts outside of health 4,8.

Generic instruments are used to measure health-related quality of life that describe the physical and mental state along several dimensions[[1]](#footnote-1) pertaining to health, by measuring the severity level[[2]](#footnote-2) of each dimension for a given health state. These instruments are required to possess good psychometric properties to be considered clinically valid and can be used to obtain population preferences for different health states. The best practice for obtaining utility scores for a given health state is to present hypothetical choice experiments (such as time-trade-off exercises) to a surveyed group of respondents that are representative of the general population. The values given by the individuals surveyed depend on their social context, culture, and personal beliefs. Some countries have invested resources in the estimation of a nationally representative set of social preference values for the health states of their population (referred to as a value set). This involves the use of generic instruments to obtain preference-based utility scores for a broad range of diseases. The collection process (in person or virtual), processing, and statistical analysis require highly specialised technical teams, funds, financing, and political will (for future use in decision-making on public health policy) 9.

The availability of a nationally representative value set for converting health states into utilities for estimating QALYs as part of CUA is important for being able to implement HTA and characterise population health priorities. The latter can help to define the prioritisation criteria used in the design of fiscally responsible health benefits plans that represent the health-state preferences of the specific society and the former ensures that technologies competing for inclusion in a health benefits plan are assessed on equal lines. Given the observed variations in preferences according to context, culture, and beliefs, obtaining estimates specific to low- and middle-income countries is essential to inform HEE in such settings.

This research article aims to be the first study in the health economics literature to contribute in a single resource, through an orderly and systematic compilation, the sum total current knowledge of the technical details of the social values of health states preferences at the national level for LMICs. To do this we performed a systematic review of the literature to identify studies that have estimated a national value set for a generic preference-based instrument for health in LMICs. The article comprises four further sections: the applied methodology, the results, and finally the discussions and conclusions derived from the findings of the systematic literature review.

1. **Methods**

We performed a systematic bibliographic search based on the recent international guidelines established by the Cochrane Rapid Reviews Methods Group 10,11. This study is registered with OSF (https://osf.io/7y6r8/). A generic search strategy was designed, which was adapted to the various sources of information. There was no restriction by type of study, date, or language. The search strategy included the documents available up to June 2022.

Keywords were identified in free terms to access non-indexed literature databases where it was expected that the greatest amount of information would be found. A strategy was executed with indexed terms (MeSH, DeCS, and Emtree) that varied according to each electronic database (Embase, MEDLINE via Ovid, CDR, INHATA, LILACS, COCHRANE). The search strategy for the databases is provided in Supplement A. In addition, we searched the web repositories of each of the health technology agencies in LMICs, as well as the websites of the various organizations leading the construction of quality of life measurement instruments internationally: EuroQol, Health Utilities Inc. and QualityMetric.

The studies included in this review contain information on the estimation of social values of health states preferences at the national level. Therefore, those articles that only included urban populations or certain types of cities that were not representative of the countries under analysis were excluded. Mendeley reference manager software was used to eliminate duplicates, and the selection process was executed in Rayyan software. Two groups of reviewers (LM, LO, and DS, AO) independently and blindly assessed each title and abstract. When necessary, a third evaluator resolved the conflicts (OE).

The same process was applied to the full-text selection. Papers included in the full-text review phase were then incorporated into the data extraction phase. The list of excluded studies and their reasons for exclusion are presented in Supplement B. Information was extracted by four reviewers (LM, LO, DS, AO) and independently verified by two reviewers (OE and LM) using a data extraction form designed in Microsoft Excel® software. The data were presented descriptively, summarising the extracted characteristics. The results were grouped according to the level of national income according to the World Bank classification for December 2022.

Finally, an expert (LM) evaluated the methodological quality using the COSMIN tool; when the need arose, the quality assessment was arranged with a second methodological expert (OE). The risk of bias assessment during a systematic literature review (SLR) assures that the results of a study are verified through the study design12. When selecting a risk-of-bias tool, specific characteristics, starting from the type of study, must be considered13. The COSMIN tool is a standardised and validated approach to guide results based on patient-reported outcome measures in healthcare, offering a comprehensive analysis of measurement properties14. It is widely used to assess primary studies and measurement properties because they are included in the same instrument, avoiding using multiple instruments simultaneously. Thus, we considered it applicable to use this approach for completing the SLR, although it inherently has limitations, as do other tools15.

1. **Results**
	1. ***Literature search results***

A total of 23630 references were found in the indexed electronic databases. Of these, 6362 (26,8%) were excluded as duplicates, and 17301 (73,2%) were examined by title and abstract. Then, 15 (0,23%) documents were evaluated in full text, of which 15 (100%) were included. Additionally, 33 articles were incorporated, which were found by reviewing the reference lists of the included articles (snowball strategy) using the *Connected Papers* platform (which uses natural language processing and deep learning techniques). Thirteen of these were excluded following further consideration. Thus, 35 documents are included in this systematic review. The PRISMA diagram that explains the process described above is presented in Supplement C 16,17,26–35,18,36–45,19,46–50,20–25. A matrix with the main fields of analysis is provided in Supplement D.

Table 1 provides a generally summary of the articles included. No studies were found prior to 2005 and most were conducted from 2013 onward 16,17,29,30,33,36,41–46,18,47,49,50,19,20,22–24,27,28. The most commonly applied method for data collection was face-to-face interview 16,17,27,32–40,18,41,45–47,50,20–26. Likewise, the studies with the largest sample size are those undertaken in upper-middle income countries 25,27,40,41,45,47,48,50,28,33–39, for which the interviews were mainly in Chinese 21,28,33,36,37,39–41, Spanish 27,38,42,47,48, or English 17–19,31,45,46,49.

Table 1. Summary characteristics of the articles

Figure 1 presents a map that indicates the number of studies providing national value sets by country, segmented by income level[[3]](#footnote-3). There are eight studies providing national value sets for China. Tunisia and Colombia have three each, while the remainder of countries with studies have either one or two. Oceania is the only continent for which there are no studies of this type for LMICs. Notably, this type of analysis has not been undertaken for any low-income country.

Figure 1. Map of the number of studies of social values of preferences of health states –representative at the national level– (low- and middle-income countries)

* 1. ***Description of instruments and preference valuation methods***

The main instrument applied was EQ-5D-5L, which was used exclusively in 15 (42.86%) of the articles reviewed 16,19,44–46,48,50,20,22,23,29–31,42,43 (see Table 2). It was followed by EQ-5D-3L, used exclusively in 12 (34.29%) articles 17,18,41,47,21,24,27,32,36,38–40. Three (8,58%) articles used two instruments 33,37,49.

All articles, except one 26, used multiple statistical models. The main model used was ordinary least squares, used in 13 (37.14%) articles 21,28,40,41,43,30–32,34–37,39. The category “other models” included those models used to a lesser extent in 9 (25.71%) articles, such as Bayesian, Fixed-effects, conditionals, censored, Tobit, and heteroscedastic models 16,22,26,28,29,32,41,42,51. Additionally, it was found that only 6 (17.14%) references 25,27,33,38,49,50 did not explicitly report the model used.

Approximately half (51%) of articles estimated a national value set using methods such as time trade-off (TTO), discrete choice experiment (DCE), composite time trade off (cTTO) or some combination of these. Seven (20%) articles used a value set from another country as a technique to measure the quality of life. The EQ-5D can be represented in a 5-digit code that defines the patient’s health states assessment. This code can be transformed into a utility weight between 0 and 1, using a set of country-specific values, estimated using instruments such as time trade-off (TTO) or discrete choice experiment (DCE). When this country-specific set of values is unavailable, some research uses another country's set of values to compute utility weights. Value sets were adopted from high-income countries (the United States 34,35, the United Kingdom 24, Poland 43, Trinidad and Tobago 45, and Uruguay 48) and one lower-middle-income country (the Philippines 49). Finally, 12 (34%) reported health states with negative utility weight that refer to chronic conditions considered worse than death are included.

Table 2. Preference valuation methods

* 1. ***Sociodemographic characteristics***

When analysing the sociodemographic characteristics reported in the included articles, it was found that 31 (88.57%) articles included age groups in their models 16,17,28–31,33–38,18,39–48,19,50,20–24,26. Of these, 10 (28.57%) were identified in lower-middle income countries. However, only 17 articles reported the mean age of the sample considered 16,21,34,35,38,43,44,47,50,23–26,28,29,32,33.

Gender data were included in mathematical modelling in 34 (97.14%) articles 16,17,26–31,33–36,18,37–46,19,47–50,20–25, 22 (62.86%) articles included information related to employment 16,17,33–37,39–41,43,44,18,45,48,49,19,23,24,28–31 and marital status 16,18,35–37,40,43,44,46,47,49,21–24,28–30,34, 31 (88.57%) articles included information related to education 16,19,30–37,39,40,20,41,43–50,21–24,26,28,29, 21 (60%) articles incorporated residence differentiated by rural and urban 16,19,31–33,36,37,40,41,45,46,48,20,49,22–24,26,28–30 (see Table 3).

Table 3. Sociodemographic characteristics

* 1. ***Utility score***

A high proportion of the studies screened did not report the estimated final utilities (see Table 4). In this regard, about 51% reported the results of the descriptive statistics of the utility estimates 16,18,42–46,48–50,24–27,29,33,36,41, and it was only possible to identify the data sets (that is, the health states, utilities, and corresponding frequency) for six (6) of the thirty-five (35) articles. Clear reporting of results is critical and represents an area for improvement in this type of literature in LMICs. Greater clarity would allow for improved replicability, as well as facilitating decisions to be informed by evidence in a more transparent manner. As previously mentioned, most of the articles reviewed used the instrument EQ-5D-5L. One study calculated a mean utility between 0 and 0.5 16, two between 0.5 and 0.9 29,46, and five a utility greater than 0.9 43–45,48,49. In the articles that used EQ-5D-3L, one had a mean utility between 0 and 0.5 17, two between 0.5 and 0.9 24,36, and one greater than 0.9 41. Finally, 63% of the articles did not report whether there were health states worse than death 16,17,42,49,18–20,22,23,28,30,31. For those countries that reported states worse than death, lower middle-income countries reported on average 13% of states (0-35%), and upper middle-income countries reported 18% (6-36%).

Table 4. Utility scores estimated

Figure 2 compares the distribution of the health states utilities among the countries. We can see that Russia 24, China 41, Indonesia 44, and Ecuador 47 have distributions skewed to the right. The data informing this figure come from the articles or their supplementary materials. In the cases where the data were were not available, we contacted the authors of the study requesting the observed utilities and their frequency[[4]](#footnote-4).

**Figure 2. Utility score distributions**

* 1. ***Risk of bias assessment***

The quality of studies was assessed using the COSMIN tool52–54, which specifically focuses on the reliability or measurement error, to inform about the quality of the outcome measurement instrument in question. Only four studies were considered adequate after the assessment using this tool 16,28,29,47. None of the studies used the statistical methods suggested by the tool and were thus considered “doubtful” in those domains 17,18,28–37,19,38–47,20,48,49,21,23–27; however, this does not mean the statistical analysis used was not suitable for this type of analysis, but highlights a limitation of the COSMIN tool. When it comes to the main observations, most of the studies used a unique measure over time 17,18,30–37,39,40,19,41–43,45,46,48,49,20,21,23–27. Supplement E contains the scores for each study.

1. **Discussion**

The continuous progress in making informed decisions by different governments, the recent impact that the HTA process has had on public policy decision-makers, and the considerable increases seen in the prices of new health services and technologies, underscore the need for countries to develop precise and robust tools and metrics to optimize the allocation of public spending on health. Societal values of health states preferences are a crucial input; however, national value sets have been estimated for a only few middle-income countries and no low-income countries. The estimation of a national value set is complicated and undertaking such analyses requires researchers with sufficient empirical and theoretical experience. It is not uncommon, therefore, to see the same authors publishing studies on this topic across different countries.

Some articles were excluded from this systematic review on the basis that the values reported were, upon scrutiny of the methodology and sampling framework used, not representative at the national level. This was generally either because rural areas were not considered or because the sample was based on people from a single city, which did not represent the diversity of the country. Although it would be ideal to have unbiased estimates of social value sets by country, certain mapping methodologies have been developed to overlap the utilities found in some countries and apply them to others. However, this is an area under development 9,55.

Historically, there has never been, and perhaps never will be, a complete consensus of the strategies to measure the preferences for health states. However, their application may play a fundamental role in conducting clinical trials, as well as in decision-making in public policy decisions on health (local, regional, and national levels). Even when instruments such as the EQ-5D are commonly used, the implications of the scale differences that arise when using different preference weighting algorithms and valuation techniques have been demonstrated in the literature 56,57. Therefore, although significant progress has been made, there is a long way to go when it comes to psychometric and clinimetric issues. Nevertheless, in the program of research to generate value sets for the EQ-5D-5L instrument, attempts were made to specify preferred methods 58.

Likewise, in this subject, although there are numerous topics to be investigated, we consider the the estimation of societal values of preferences for health states in children and adolescents to be a priority. In the initial phase of development, this field of study may add significant value to the application and subsequent validation of cost-effectiveness studies for these age groups.

Ultimately, the estimation of societal values of health states preferences at the national level represents an important area of research with the potential for high impact through its application in HEE. HEE in HTA may be used to inform decisions by countries to fund (or not fund) health technologies, health benefits plan updates, drug pricing, health procedures pricing, complementary social services pricing, and more, all with implications for population health. Studies of this nature should therefore be developed in consultation with the governing body of the respective country's health system and should be a priority for governments where they are not currently available.

1. **Conclusion**

Among the main findings of this study is that nationally representative social values of health states preferences are available for only 19 out of 82 LMICs classified by the World Bank. However, there are multiple studies for some of these countries, for example, China stands out as having eight. Where there are multiple available studies (as is the case for Sri Lanka, Thailand, Philippines, Indonesia, Russia, Colombia, Tunisia, and China) the choice of which values to use is a judgement best left to researchers because, as with preference assessment methods or health outcome measures, there is no metric that reliably defines the absolute superiority of one option or another.

The reporting of data on these studies is not standardised in the literature, and researchers may wish to consider that the transparency with which finding are reported when choosing. For instance, in Colombia, there are three studies, but only one reported the utility scores estimated.

The most frequently applied generic instrument to measure health-related quality of life was the EQ-5D-5L and the ED-5D-3L, with face-to-face interviews being the most common form of administration. The statistical methods most frequently used to study health-related quality of life values were ordinary least squares, generalized least squares, Tobit, and logit, as well as hybrid approaches. In contrast, the Bayesian approach was only used in two studies. Finally, our study shows that characteristics such as old age, low levels of education and income, and marital status (widowed or divorced), among other characteristics, have a negative role in peoples’ health utility.

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1. Dimension pertain to different aspects of quality of life, for example: physical functioning, role limitations, social functioning, pain, mental health and vitality59. [↑](#footnote-ref-1)
2. For example: no problems, slight problems, moderate problems, severe problems, and extreme problems59. [↑](#footnote-ref-2)
3. Regarding the funding sources for the development of these research projects, at least18 articles were financially supported by the governments, at least 8 were supported by academia and the Euroqol Research Foundation, only 3 were supported by the pharmaceutical industry and 5 were not financially supported at all. [↑](#footnote-ref-3)
4. In total 46 emails were sent on 18 September of 2022 to the different authors of the selected papers. Only 12 emails were responded to and 5 were bounced. Of the 12 responses obtained: some sent the information but did not have the frequency data needed to make the graph, some made reference to the supplementary material of the article, some asked to consult other authors or EuroQol office, and in some other cases authors stated that they did not have the information available. The last response was on October 3, 2022. [↑](#footnote-ref-4)