

# Identifying Priority Methodological Issues in Economic Evaluation in Low- and Middle-Income Countries: Finding the Holy Grail

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## List of Abbreviations

AfHEA	African Health Economics and Policy Association
AFR	WHO Africa Region
CEESTAHC	Central and Eastern European Society of Technology Assessment in Health Care
CADTH	Canadian Agency for Drugs and Technologies in Health
CBA	Cost-benefit analysis
CEA	Cost-effectiveness analysis
CHEER	Consolidated Health Economic Evaluation Reporting Statement
CRD	Center for Research and Dissemination
CUA	Cost-utility analysis
DALY	Disability-Adjusted Life Years
EMR	WHO Eastern Mediterranean Region
EU	European Union
EUnetHTA	European Union Network for Health Technology Assessment
EUR	WHO Europe Region
GDP	Gross Domestic Product
HIC	High Income Country
HITAP	Health Intervention and Technology Assessment Program
HTA	Health Intervention Assessment
HTAi	Health Technology Assessment international
HTAsiaLink	HTA network in the Asia region
iDSI	International Decision Support Initiative
INAHTA	International Network of Agencies for Health Technology Assessment
ISPOR	International Society for Pharmacoeconomics and Outcome Research
LMIC	Low- and Middle-income Country
MCDA	Multiple Criteria Decision Analysis
NICE	National Institute for Health and Care Excellence
PAH	WHO Americas Region
PLOS	Public Library of Science
QALY	Quality-Adjusted Life Years
RAHEE	Research Methods Agenda for Health Economic Evaluation
RCT	Randomized Control Trials
RedETSA	Red de Evaluación de Tecnologías en Salud de las (HTA network in the Americas)
SEA	WHO Southeast Asia Region
SDG	Sustainable Development Goals
UHC	Universal Health Coverage
WHO	World Health Organization
WPR	WHO West Pacific Region

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## Executive Summary

There is increasing demand for economic evaluation in healthcare policy making. However, the use of economic evaluation studies is limited, especially in low- and middle-income countries (LMICs), although the need for such evidence in decision making is arguably higher for LMICs since they face more constraints and limited resources than countries in high-income settings. A literature review found that methodological quality is lower in LMICs than in high-income countries which limits the use of this kind of study. This project was initiated through the international Decision Support Initiative (iDSI) in order to identify the issues that limit the quality and the use of economic evaluations. From the priority list of issues finalized from the study, potential solutions and research questions were derived on how to solve the issues.

The following report details the study results, which was completed in two parts. In the first part of this study, a literature review of methodological issues was conducted. This then informed the second part of the project in which data was collected through a survey. The survey was sent to researchers from around the world for inputs based on their perspective and experience in conducting economic evaluations in LMICs. Across all settings, the majority of the survey respondents reported that the most important technical issues facing researchers are the lack of quality local clinical data, poor reporting, and insufficient cost data to conduct the analysis from the chosen perspective. Some of the proposed solutions and research questions involved developing standard guidelines, procedures, and practices for gathering data (clinical, utility values, costs, etc.), reporting, and other issues that may be adapted to or used in LMIC settings. While there are already some guidelines and methodologies developed, it may be worthwhile to explore their use on a national, regional, and global level. In addition, other practices such as transferability could also be explored. Given that these issues were also frequently cited, the report discusses some context-specific issues that affect research, such as limited capacity to conduct economic evaluations.

With the preliminary results analysed, a stakeholder consultation for the project was held to discuss the findings of the technical work and to explore the ways in which the research and its outputs could be used as a resource for researchers and students globally. The results were well-received, with participants placing an emphasis on ensuring that research questions for technical issues can be separated from context-specific issues. The consultation also discussed the online database, which will be launched in the last quarter of 2016 and display results from the report. Further, the database will be a continuation of the project with have several features, the primary goal of which is to address common issues that researchers face and provide solutions promptly.

## Introduction

With the dawn of the era of the Sustainable Development Goals (SDG), the importance of universal health coverage (UHC) has become increasingly prominent. Under the SDG Goal 3 is Target 3.8, which states that countries must “[a]chieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all [1].” Internationally, this push is taking root: there was a report that 75 countries had legislation to move towards UHC while 58 of these countries, of which 22 were LMICs, had achieved UHC in 2006-2008 [2]. This highlights UHC’s importance in all settings, wherein countries are recognizing that it is part of their development to ensure that the governments provide the health services needed without putting undue financial strain on both their people and themselves. Constraints in terms of limited health care resources then become the major challenge that countries must face, regardless of income level, so much so that the global movement towards UHC is supplemented with finding ways to effectively set priorities for health systems.

Health technology assessment (HTA) is one of the tools for priority setting, which “refers to the systematic evaluation of properties, effects, and/or impacts of health technology. It is a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology. The main purpose of conducting an assessment is to inform a policy decision making... [and is applied to] medicines, medical devices, vaccines, procedures and systems developed to solve a health problem and improve quality of life [3].” More and more countries are using HTA for their national decision making processes, and the World Health Organization (WHO) has passed a resolution to endorse and call for commitment from Member States to use HTA [4]. Economic evaluation is a tool used in HTA that is garnering significant attention due to its ability to inform about cost-effectiveness, i.e. efficiency, and therefore to assist in decision-making on setting priorities in healthcare which is a challenge that countries face in terms of achieving UHC.

Many countries that weaved HTA in their priority setting processes have embarked on using economic evaluation as well, and its knowledge and use is diffusing rapidly over the world. However, there are still barriers, especially in LMICs, to the use of economic evaluation evidence to inform policy decision-making, e.g. limited availability, limited quality and limited relevance of such evidence in the context. Evidence from economic evaluations is rarely integrated with policy and this can result in inadequate availability and quality of the evidence in the sense that there is no formal mechanism to support its use and a strong political demand for improvement of the quality and quantity of work. Despite this, effective and rigorous standards for economic evaluation methodology, guidelines, and protocols are essential to ensure that policy-makers can be provided with the best available evidence and therefore slowly generate support and buy-in from stakeholders and decision makers.

Although there are methodological guidelines widely available, the guidelines are mostly developed for use in high-income countries (HICs) and where they are developed in LMICs, they usually follow recommendations in the HICs guidelines which are not necessarily applicable or effective in LMICs. This may be due to the fact that economic evaluations are used more widely in HICs and therefore limited normative works focusing on methodological development of economic evaluation conducted in LMICs are available. For example, the unavailability of studies on willingness-to-pay thresholds in some countries results in the lack of decision rule to consider the cost-effectiveness each health technology or intervention offers. To break the loop, enhanced quality of evidence is warranted. Firstly, gaps, that may be related to the process, context or technical in nature, preventing researchers from generating high quality economic evaluation evidence need to be identified and filled, e.g. through research that focuses on resolving the challenges in the conduct of economic evaluation and to provide assistive tools for researchers. The improved tools lead to higher quality evidence and better decisions given capacity to generate and to use such evidence when available. This will call for

sustainable generation of evidence and even higher quality and usability of evidence. Figure 1 illustrates the cycle as the Theory of Change of Methodological Research Development.

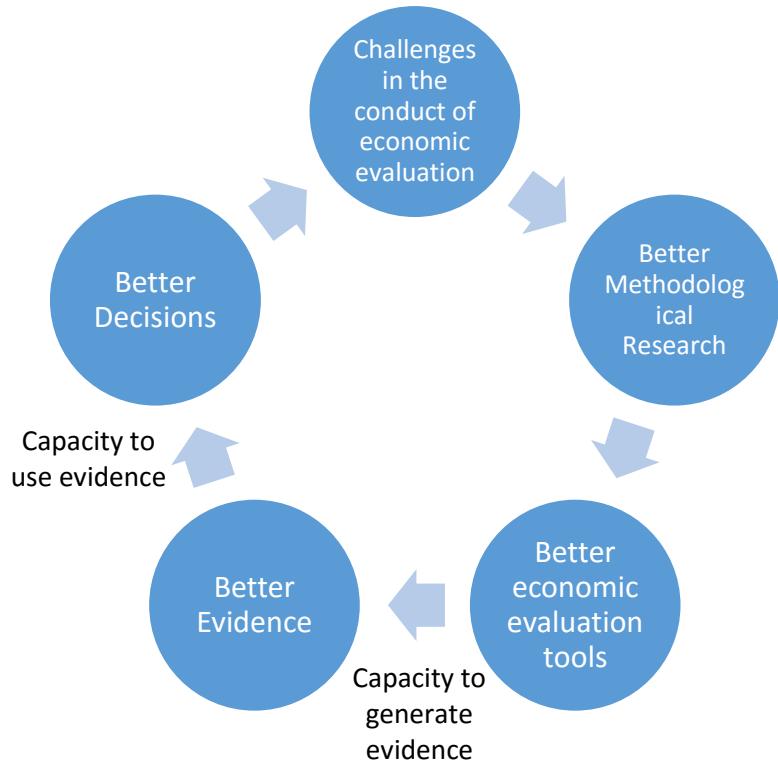


Figure 1: Theory of Change of Methodological Research Development

There had been attempts to identify these gaps and challenges. However, majority of the research is disease-specific, country-specific or without a focus on LMICs [5-27]. In 2013, the Research Methods Agenda for Health Economic Evaluation (RAHEE) was conducted in Europe, with the aim of “providing an outline of existing evidence for 10 high burden conditions in the European Union (EU)... [as well as] insight into the institutional factors and best practices associated with the use of economic evidence in the field of preventive and public health [28].” While this research has been conducted in the context of the EU, there is a dearth of research specific to LMICs and the obstacles that these countries face in using economic evaluation.

The iDSI, an international mechanism to provide policy-makers at the sub-national, national, regional and international levels with coordinated support in priority-setting as a means to UHC, is keen to assist these countries by conducting a normative research to identify the agenda for research which needs to be filled in order to achieve better quality economic evaluations. This study aims to achieve this, beginning with a comprehensive review of literature identifying issues for conducting economic evaluations to learn about the current issues that prevent the generation of quality evidence. The issues identified from the review were used to inform a survey sent to international scholars working all over the world who have conducted economic evaluation in LMICs in order to prioritize the issues as they have observed in their work. Results from this survey were analysed and outlined as prioritized gaps which were discussed in a face-to-face consultation meeting with policy-makers and HTA practitioners working in LMIC settings in January 2016. This project has two main outputs which will showcase the results and additional research in different ways: the study and the database. The final results after discussions will be inputted into an electronic database to inform the global community since to ensure all the issues are addressed in the future, combined effort is crucial. The database will

be updated biennially to facilitate the sustainability and accuracy of the methodological issues that need to be addressed for LMICs.

This research ultimately aims to assist countries (as well as those from outside working in these countries) in using HTA in their priority setting processes, while building knowledge and capacity for HTA.

## Methods

### Study design

The survey was conducted in the form of a web-based survey questionnaire, and was constructed based on expert opinion and a literature review.

### Literature review

In order to develop a questionnaire, potential issues that might be hindrances to the conduct of economic evaluation in low- and middle-income settings were identified through the review of literature in PubMed and Center for Research and Dissemination (CRD) databases.

Key publications discussing the barriers, flaws or difficulties in the conduct of economic evaluations were retrieved from PubMed and supplemented by reference search. The issues in both high-income and low- and middle-income settings were included since although there were differences in the stage of the research between these settings, the issues in the high-income settings also tended to exist in the low- and middle-income settings. Twenty-five key studies were included and reviewed for the issues.

The CRD database was also employed owing to its critical appraisal of economic evaluation studies. From the CRD, primary economic evaluations of which a commentary is available were identified through the search of LMICs name based on World Bank classifications as of 2015. The search returned 568 hits of which 180 studies were done in low-and middle-income settings. Of these, commentaries of 100 studies were randomly selected for review of the criticism on its technical problems and weaknesses. The issues identified from the review were summarised and categorised based on particular types of technical issues: on interventions/comparators (e.g. did not use standard comparator), study population (e.g. no mention of randomisation), effectiveness/benefits (no sensitivity and specificity), costs (e.g. discounting not used even when appropriate), and analysis and results (e.g. no discussion on limitations and/or transferability).

### Scope of the study

The project focuses on methodological issues in economic evaluations. Methodological issues are defined as issues that affect the methods and the conduct of economic evaluations. The issues can be grouped into technical issues and context-specific issues. For the purpose of this study, technical issues will be considered as those that directly link to the methodology of economic evaluation and can be solved through changes in the methods or to have methodological or reporting specifications. On the other hand, context-specific issues are those that indirectly affect the conduct of the study and are more bound to the situation in the context, i.e. not easily changed with minor adjustment in the conduct of the study. An example of the context-specific issues is no systematic process of considering economic evaluation evidence. As such, the questionnaire was divided into two main parts: technical issues and context-specific issues in order to address any issues that may affect the quality of research or its relevance to policy.

## Questionnaire

The first part of the questionnaire focuses on the details of respondents' demography (response rate, educational attainment, years of experience, geographical areas of work, geographical distribution of respondents, and affiliation). For both technical and context-specific components, the respondents were asked to consider the list of issues provided, add an issue that they thought was relevant but not yet on the list, and rank the top 3 technical issues and the context-specific issue that they considered most important in their contexts. They were also asked to propose possible solutions and to choose whether the technical or the context-specific issues were more important. Information on similar projects elsewhere was also requested in order to use as an input for future development of this project.

A pilot was sent to approximately 10 academic peers for their comments and review. This questionnaire was then revised and sent out online.

## Study population

The study population comprised researchers who had completed at least one economic evaluation project as the primary investigator or as a part of a team in low- and middle-income settings. The low- and middle-income settings are defined according to World Data Bank classifications as of 2015. To recruit respondents, both individuals and networks were approached. Invitation to participate in the survey was sent to the secretariat of health economic and outcome research networks as well as various health technology assessment networks in different regions for the secretariats to distribute the survey to their members. The participating networks included the African Health Economics and Policy Association (AfHEA), HTA Network of the Americas (RedETSA), and HTAsiaLink. There were no responses from Central and Eastern European Society of Technology Assessment in Health Care (CEESTAHC), European Union Network for Health Technology Assessment (EUnetHTA), and Health Technology Assessment international (HTAi) secretariats while the International Society for Pharmacoeconomics and Outcome Research (ISPOR) the International Network of Agencies for Health Technology Assessment (INAHTA) declined to participate. Individuals were also identified through snowball approach (existing respondents recruit future respondents from their network). In total, there were 927 recruited respondents. However, since the mailing lists of each network are classified and respondents were mostly contacted through the network as a whole, there is a possibility of duplication which cannot be eliminated and the exact number of recruited respondents may be less than the figure shown.

## Data analysis

The top priority issues for technical and context-specific issues have been analysed separately. Since there is more than one issue ranked for technical issues, in order to rank the top priority issues, a system similar to Likert scale was applied. For each response, the technical issue that was ranked first would be assigned the score of 3, 2 for the second rank, and 1 for the third rank. The score for each issue in the components was then ranked in a league table to derive the list of top priorities. Where there was more than one issue that received the same score, their frequencies in ranking amongst the higher levels would be considered.

The results of the ranked issues were then analysed as a whole, by the WHO regions, and by the respondent affiliation and experience. The solutions that fell within the same concerns or areas or same direction were grouped together. Moreover, the issues and the solutions were examined for any connections or relationship, and the means to achieve the solutions were proposed.

## Stakeholder consultation

A stakeholder consultation for the project was conducted with the following objectives: to discuss the findings of the technical work, to explore the ways in which the research and its outputs can be used as a resource for researchers and students globally, and whether the database, one of the outputs of the study, can address common issues that researchers face and provide solutions promptly. The consultation was conducted at the Health Intervention and Technology Assessment Program (HITAP), Thailand, on January 25, 2016. The attendees consisted of research and local partners from various countries and organizations, including Ministries of Health, HTA agencies, and the WHO (please see Appendix 3 for more information).

## Results

### *Literature review results*

#### **Result from the review of key publications about the issues in the conduct and the use of economic evaluations**

Issues were identified from 25 key publications that focused primarily on methodological issues in the conduct of economic evaluations and examined for its frequency of mention (Table 1). Among these publications, the issue mentioned most frequently was poor reporting (9 studies). The next most frequently mentioned issue was the lack of high quality local clinical data (7 studies). The lack of local utility data (4 studies) and the inappropriate characterization of uncertainty (4 studies) were also issues of concern. Context-specific limitations were less discussed in the included studies. When these issues were discussed, the issues highlighted were the lack of the inclusion of economic evaluations in decision-making; limited local research capacity; limited number of journals with high quality review process; and misunderstanding between researchers, academia, and policy-makers.

Table 1: Frequency of issues being mentioned in included key publications from PubMed (n=25)

Issues	Number of Studies Mentioned
Technical issues	
Poor reporting	9
Perspective not stated	7
Methodology not presented in a clear and reproducible manner	2
Disaggregated result not presented	1
Funding sources not reported	1
Ethical issues are discussed	1
Lack of high quality local clinical data	7
Lack of local utility data	4
Sensitivity analysis not properly characterized	4
Some relevant cost data omitted	3
Incremental analysis not performed	3
Clinical data not based on systematic review	2
Lack of reliable cost data	2
Discounting not performed, if relevant	2
Methodology lacks standard, transparent methods	2
Comparator not appropriate	1
Variations among costs, effects, and cost-effectiveness data within and between settings	1
No objective budget constraints or threshold applied	1
No reference case specific to developing contexts	1
Context-specific issues	
Economic evaluation is not included in a formal process to support decision-making process	1
Limited local research capacity	1
Limited local good quality journal with a high standard process of review	1
Misunderstanding between researchers, academia and policy-makers	1

## Results from the review of 100 randomly selected publications from CRD database

Most of the studies from CRD database that were selected for review were published after 2000. Of these, the most number of studies were published in 2011 and 2012 (13 studies each), followed by 2001 (10 studies) (Figure 2).

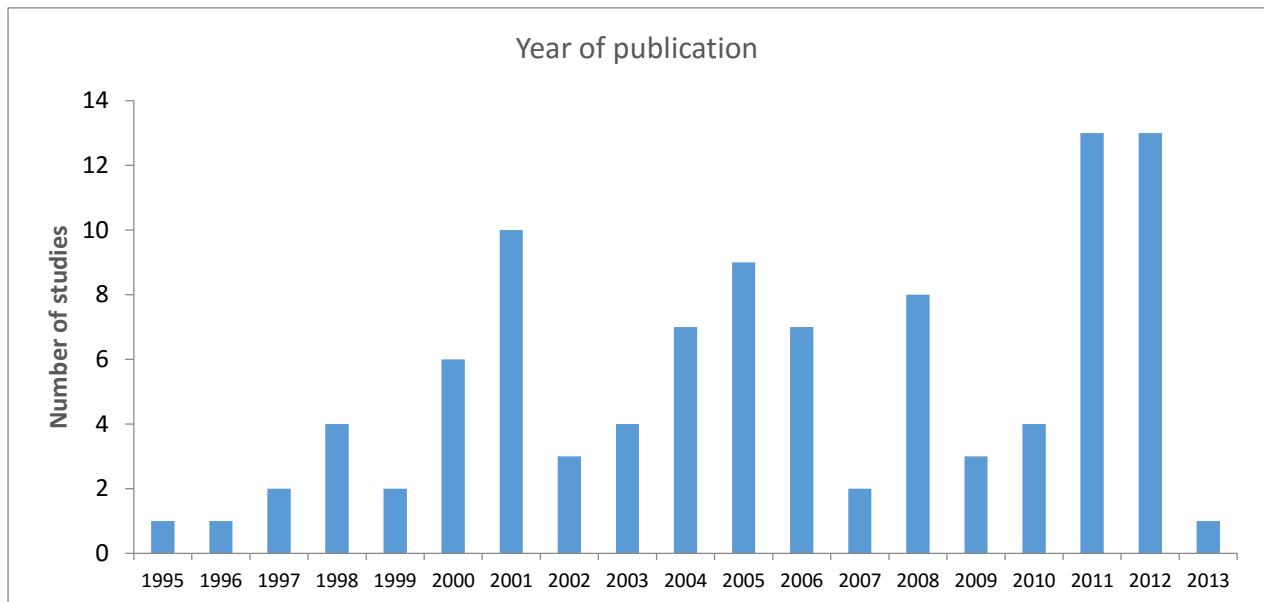


Figure 2: Number of selected studies published in each year (n=100)

Majority of the studies reviewed were cost-effectiveness studies, which accounted for 58% of the total (58 studies). Cost-utility studies accounted for 38% of total studies reviewed (38 studies). On the other hand, only 4% of the studies were cost-benefit analyses (4 studies). (Figure 3)

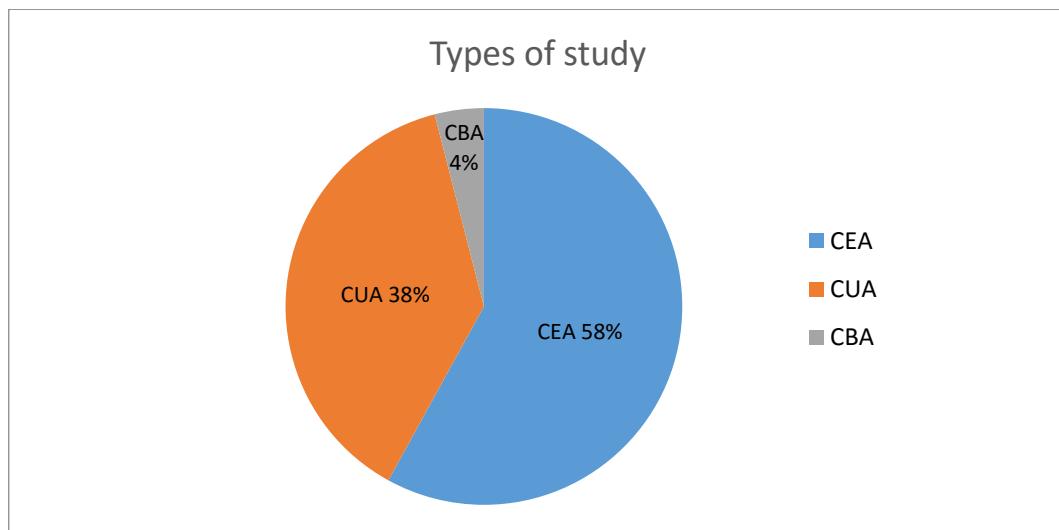


Figure 3: Types of selected studies reviewed (n=100)

The journal that published the most number of selected studies was Vaccine (5 studies). The next highest number of selected studies were found in *Value in Health*, *Tropical Medicine and International Health*, *Journal of the Medical Association of Thailand*, *PLOS Medicine*, *AIDS* (3 studies each).

The issues found from the review of randomly selected CRD studies were also counted and ranked based on frequency (Table 2). As with the review of publications in Pubmed, poor reporting was cited

as the most frequently found issue (81 studies). The next most frequent issues encountered were the absence of consideration of a threshold (78 studies) and the absence of incremental analysis (41 papers), the absence of sensitivity analysis (38 studies).

Table 2: Issues in selected studies from CRD database (n=100)

Issues	Numbers of Studies in Which the Issue is Found
<b>Poor reporting</b>	<b>81</b>
Perspective of analysis not stated	37
Price year not reported	37
Decision model not described, if relevant	21
Limited details on utility/disutility data	15
Source of cost data not given	12
Discount rate for cost not given	12
Limited details on source of effectiveness data	11
Limited details on disaggregated cost data	11
Sources of effectiveness data not given	7
Not clear whether all relevant options were included	5
Details on study population not given	5
Justification of the comparator was not provided	4
The comparator was unclear	3
Details of comparators were not provided	2
Unclear whether discounting is done for effectiveness	2
Discount rate for effectiveness not given	2
Details on intervention is not provided	1
Unclear whether discounting is done for cost	1
Limited details on currency conversion	1
No specific threshold applied	78
Incremental analysis not performed	41
Sensitivity analysis not performed	31
Health measures used not appropriate	28
All relevant evidence not included	17
Discounting of cost not appropriately done	16
Sources of effectiveness should be improved	11
Some relevant costs are omitted	7
Charges used instead of cost	4
Sources of cost data should be improved	3
Discounting of effectiveness not appropriately done	2

## *Survey results*

The results were divided broadly into the following sections: respondent information and background, analysis of priority issues, proposed solutions, and a supplementary section on related studies.

### Respondent Information

#### **Response rate**

In total, the survey was sent to 927 potential respondents. Of these, 349 were from AfHEA, 69 were from RedETSA, 326 were from HTAsiaLink and 183 were individuals whose demographic information is not available. Of these, 178 people responded to the survey (19% response rate). Among the respondents, 125 people were found to be qualified to provide their perspective based on their response to a “qualifier question”, see Figure 1. Of the 125, 110 respondents gave their permission to use their responses for the research and proceeded to answer the survey; however, some respondents did not answer all questions and the number of responses for some questions may be less than 110.

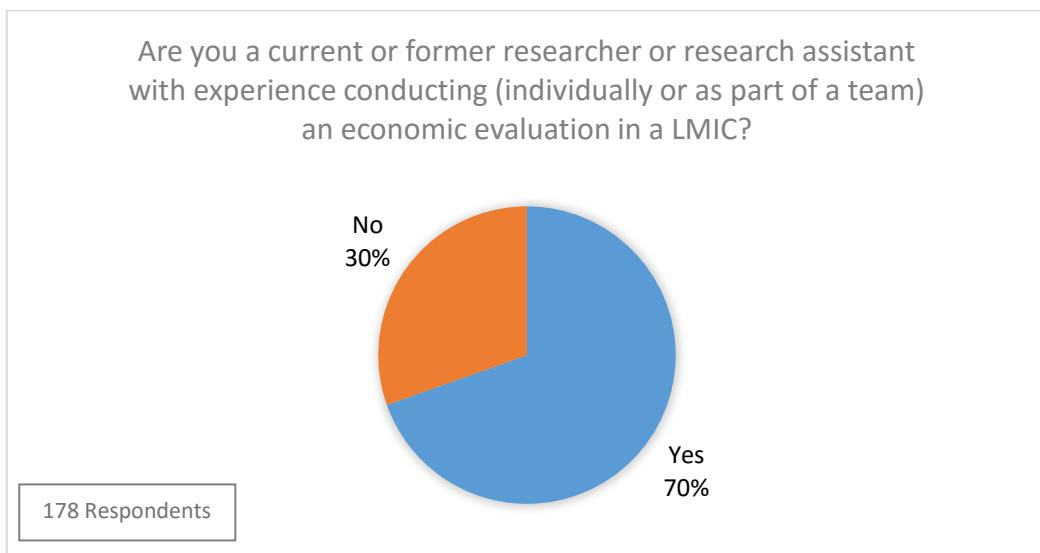


Figure 4: Qualifier for the survey respondents

## **Background**

Most respondents have a graduate degree (90%) and of these, 53% have a master's degree as their highest degree while 37% have a doctorate. (Figure 5)

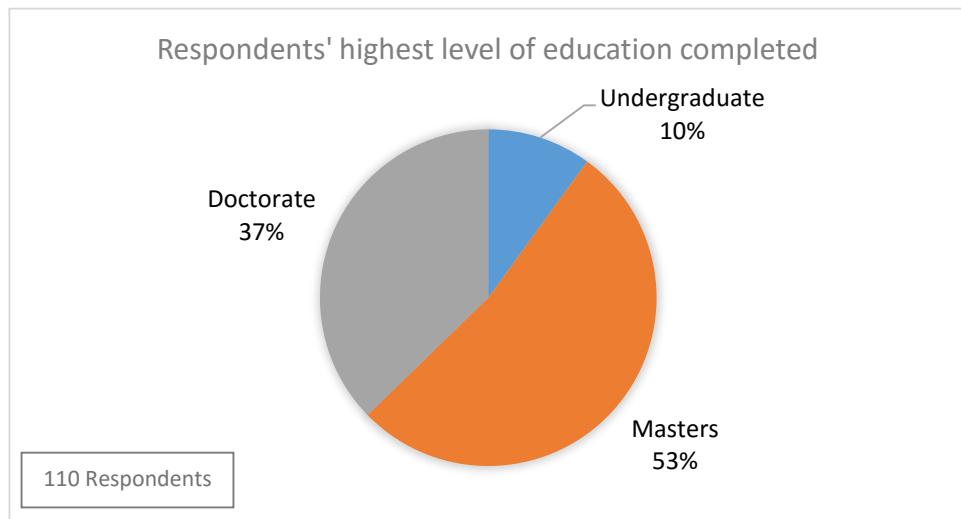


Figure 5: Highest level of education completed

For 64% of the respondents, economic evaluation was a major part of their education, while for 36% of the respondents, it was not. (Figure 6)

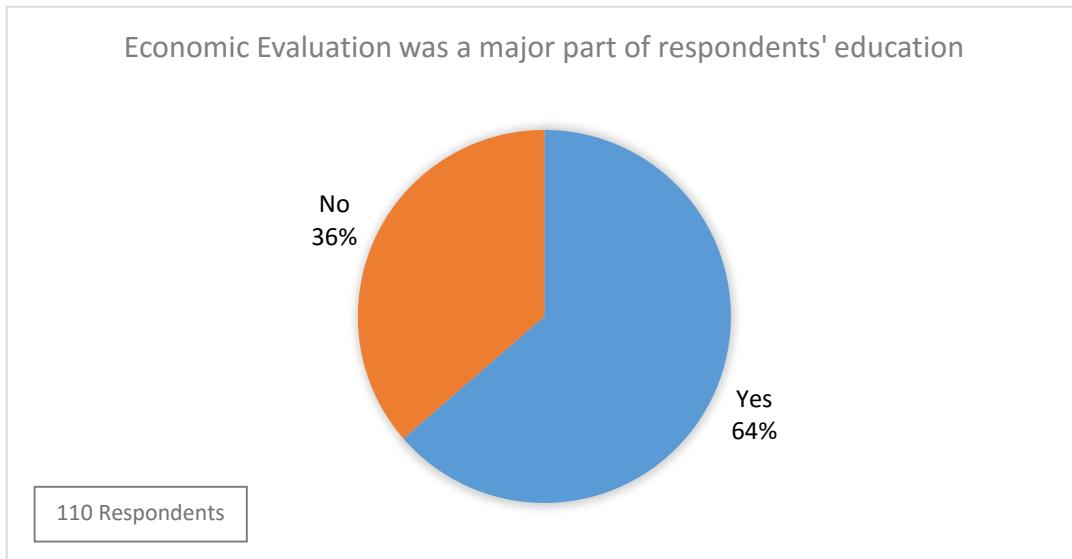


Figure 6: Economic evaluation was a major part of their education

## **Experience in the field**

A majority of respondents, around 53% of respondents, had 6 or more years of experience in economic evaluation, while 47% had 5 or less years of experience. (Figure 7)

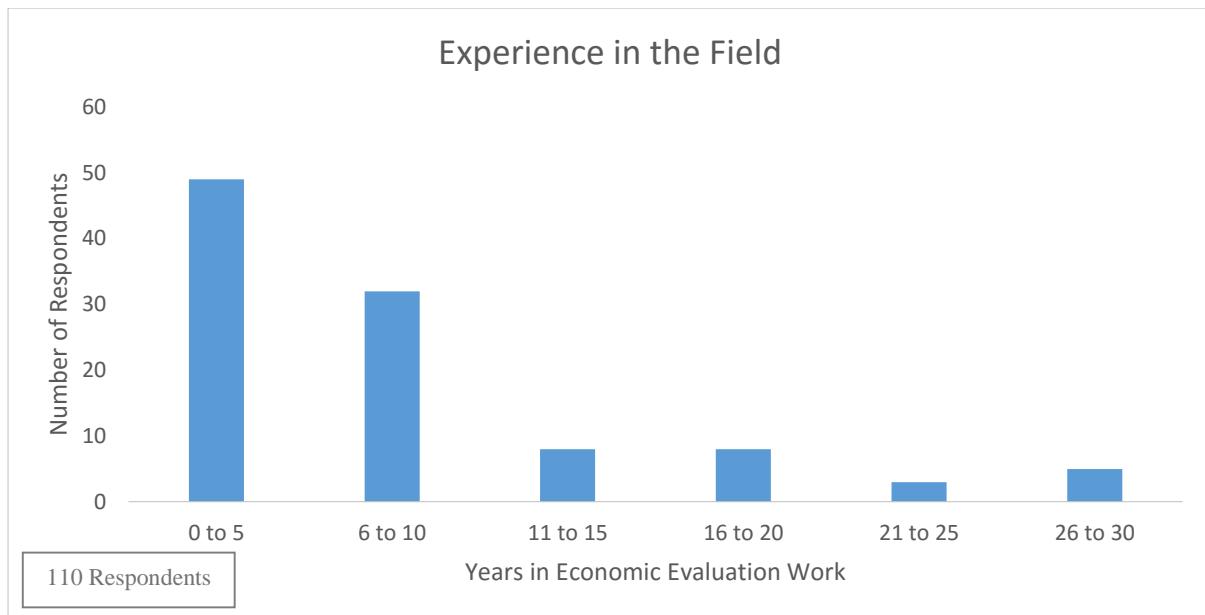


Figure 7: Years of experience in economic evaluation

#### Responses per Region

21% of respondents came from Southeast Asia (SEA), 15% came from Africa (AFR), 20% from the Americas (PAH), 15% from Europe (EUR), 2% from Eastern Mediterranean (EMR), and 28% from West Pacific (WPR). (Figure 8)

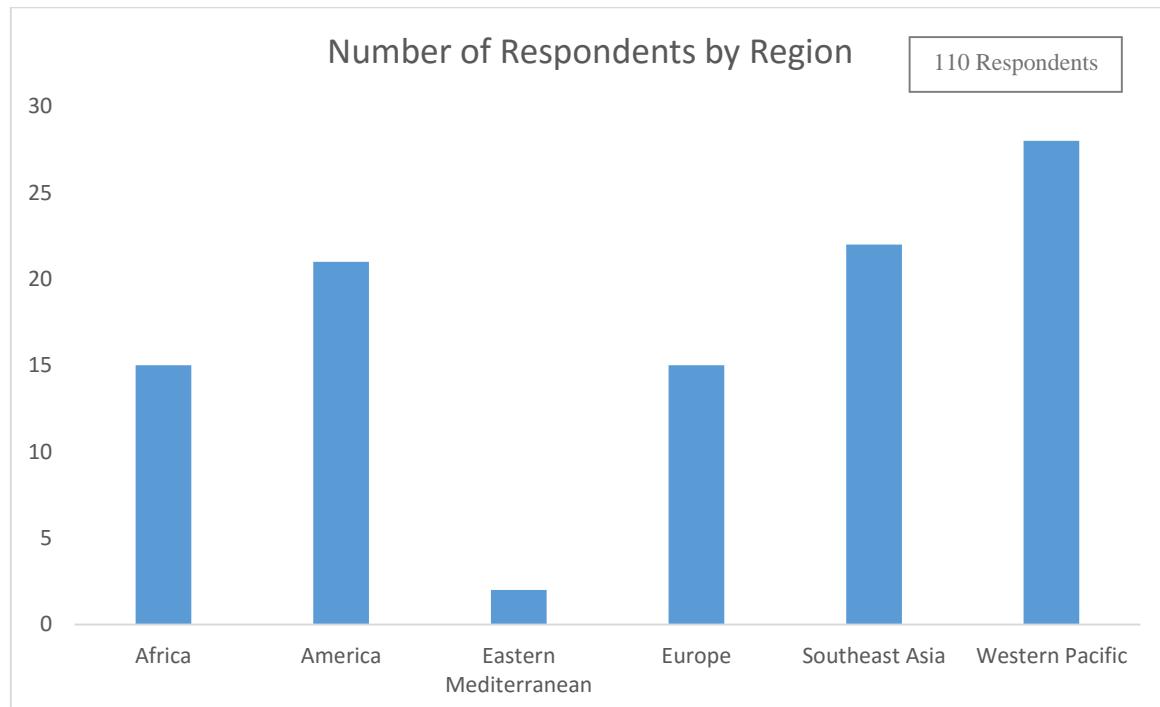


Figure 8: Respondents per region

## Affiliations

Considering affiliation, 42% of respondents were from the academia, another 42% were from public health institutes. Six percent were from government research agencies and 6% from ministries of health. Four percent were from unspecified governmental bodies, consultancies, and industry. The other 4% were from other organizations, i.e. a hospital, a private company, a national health insurance program, and a multi-lateral agency. Since respondents were allowed to select more than one type of affiliation, the total proportion exceeded 100%. (Figure 9)

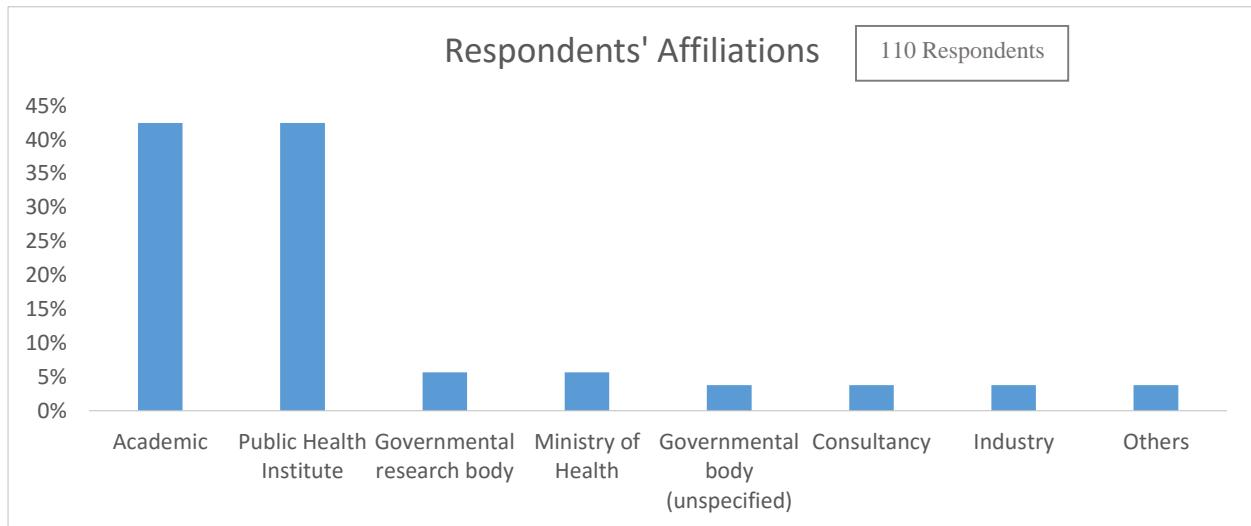


Figure 9: Respondent affiliations

In terms of the affiliation of respondents by region, respondents from AFR and EUR were mostly from the academia (52% and 79%, respectively). On the other hand, respondents from SEA and WPR were mostly from public health institutes (63% and 38%, respectively) while the respondents from PAH and EMR were equally from the academia and public health institute. (Figure 10)

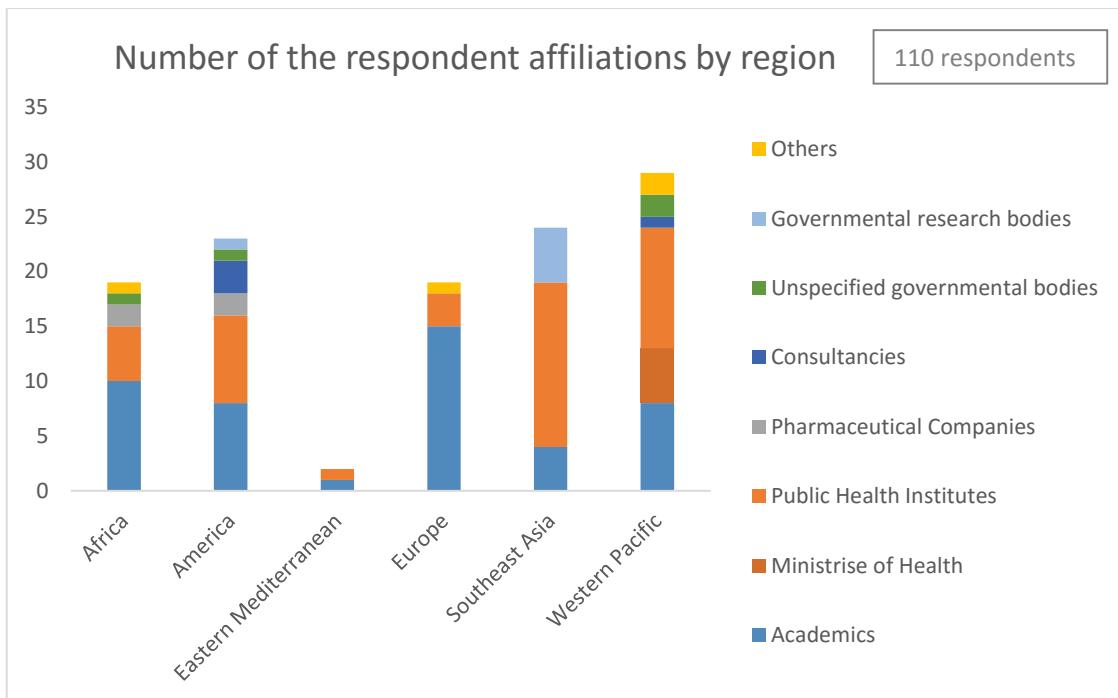


Figure 10: Respondent affiliations by region

Most respondents work in their home regions, although some work in regions other than theirs. For example, many respondents from PAH (14 respondents) reported working in SEA (8 respondents), AFR (7 respondents), EUR (5 respondents), and the WPR (6 respondents). Respondents from EUR (12 respondents) also work in SEA (5 respondents) and AFR (12 respondents). Similarly, some respondents from WPR (23 respondents) also work in SEA (6 respondents). (Table 3)

Table 3: Respondents from other regions working outside their own

<b>Home Region of Respondents</b>	<b>Respondents Working in Southeast Asia</b>	<b>Respondents Working in Africa</b>	<b>Respondents Working in America</b>	<b>Respondents Working in Europe</b>	<b>Respondents Working in the East Mediterranean</b>	<b>Respondents Working in West Pacific</b>
Southeast Asia	23	1	1			1
Africa		14		1		
America	8	7	14	5	2	6
Europe	5	12	2	12	2	3
Eastern Mediterranean					2	
Western Pacific	6					23

## Priority Issues

The most important technical issues are lack of essential clinical data, poor reporting, and insufficient data to conduct the analysis from the chosen perspective. Lack of high-quality local clinical data is different from insufficient data to conduct study from the chosen perspective, i.e. lack of some cost data. The context-specific issues that emerged are non-inclusion of economic evaluation in the decision making process, limited local capacity to conduct the research, and lack of funding. (Table 4)

Table 4: Priority Technical and Context-Specific Issues

	<b>Technical Issue</b>	<b>Context-Specific Issue</b>
1	Lack of high quality local clinical data, where such data are critical to the decision	Economic evaluations not included as a part of the decision-making process
2	Poor Reporting: <ul style="list-style-type: none"><li>• Perspective of analysis not stated</li><li>• Lack of details of the target population or sub-populations relating to the interventions being evaluated</li><li>• Lack of detail on the methods used to derive the measure of benefit</li><li>• Lack of details to enable checking of data sources for benefits / effectiveness</li><li>• Lack of details to enable checking of data sources for costs</li><li>• No details of the price year used as the basis of the cost analysis</li><li>• Methodology not presented in a clear and reproducible manner</li></ul>	Limited local capacity to conduct or contextualize research
3	Insufficient data to conduct study from chosen perspective	Lack of funding for the necessary research
4	A lack of commonly accepted standards for economic evaluation that's relevant to the LMIC for which the analysis is undertaken	Misunderstandings and communications weaknesses between researchers, academia and end users of the evidence
5	Absence of locally-relevant health state preference data suitable for estimating QALYs or DALYs	Absence of local journal with a high quality reviewing processes
6	Inappropriate choice of comparator (s)	
7	No budget constraints or thresholds considered	
8	Generalizability not discussed	
9	Clinical data not based on systematic review; or primary clinical data not compared with similar studies done elsewhere	
10	Equity and/or gender implications not considered	
11	No incremental analysis	
12	OTHER	
13	No, or inappropriate, sensitivity analysis	
14	All impacts implied by the chosen perspective not investigated	
15	Uncritical use of charges for cost data	
16	Time horizon too short to capture relevant costs and health effects	

Technical issues, under OTHER in the questionnaire, were added to the results and summarized. The technical issues cited were: lack of evidence of health opportunity costs and willingness-to-pay thresholds, lack of comparators, inappropriate choice of model, and issues with the design of research. Some of the issues cited involved pre-HTA work, e.g. having a feasibility study for new technology and determination of market share for new technologies.

Most of the technical issues identified above overlap with context-specific issues, and respondents specified these points detailed in the following paragraph. One was lack of experts in the field as well as lack of skills in interpretation of results and presenting them to stakeholders. Policy-makers do not understand the use of HTA, resulting in low demand and inability to translate findings into action. One respondent was concerned about the limitations of the use of economic evaluation itself, and suggested exploring other approaches such as multiple criteria decision analysis (MCDA), and noted the importance of having a process which is transparent, timely, and participatory. Another respondent mentioned that the lack of the HTA process often results in a conflict of interest (pharmaceutical industries conduct their own research) and difficulties in selection of an HTA topic. Other respondents mentioned that even the budget impact is not usually analysed and presented to stakeholders; if there is an analysis, there are frequently issues in the conduct of the budget impact analysis. It is also difficult to implement intervention at scale, and there is lack of real-world data on implementation barriers. Another issue was that non-financial constraints (i.e. the lack of core health system inputs, such as qualified human resources for health, facility/access infrastructures etc.) is another important consideration that likely affects the conduct of cost-effectiveness of many interventions in resource constrained setting.

Related to the technical issues, respondents also note these points. There is a lack of priority setting and coordination among evidence producers at the national level. There is lack of capacity in health care for proper technical economic modelling, as well as capacity to appraise the results / papers. Even when good results are available, there are few forums to share these at the national level. High income health economists and academics in developing countries have little collaboration, limiting information exchange and transfer.

The most important issue in the survey is the quality of data, and this is reflected in the open-ended answers from respondents as well. There can be issues of lack of representativeness or over-generalization. Poor information system at the provider level and communication among different stakeholders to provide data for assessment were cited. There is poor or no information about costs, with multiple cost data sources (while all are "correct," there is not a single chosen cost data source acceptable to all stakeholders). Distribution of costs and benefits are not addressed, e.g. in workplace interventions, costs commonly fall mainly on owners and benefits on workers. Further, there is lack of access to software for data management.

For other context specific issues with open ended answers, the respondents gave the following responses in the questionnaire. One of these is that there is an unclear target audience for economic evaluation in some settings. There needs to be more clarity about opportunity costs and how CEA helps. In the settings that use economic evaluation, there is often a high focus on CEA, which can be too narrow. The relevance of economic modelling versus budget impact is also an issue. Decision makers may have limited knowledge of HTA and want specific answers without understanding the analytical context. In addition, the research agenda may be driven by political and economic forces, rather than local need, and there may be favouritism amongst policy-makers. There may be lack of accountability in the decision making process in LMICs, as well as lack of transparency in the use of economic data in the decision making process. There are also often changing priorities with changes in leadership. Additionally, a well-informed official/ministerial demand for systematic priority setting methods may not be present.

### **Geographical Comparisons**

The issues were prioritized based on responses from respondents who work in the region (not necessarily only those who are from that region). Considering each region separately, of the priority issues, the lack of high-quality, local clinical data is the one that is noted as the most important issue for SEA, PAH, and EMR, and the second most important issue for AFR. In addition to this, insufficient data to conduct the study from the chosen perspective was also noted for almost all regions except for WPR. Poor reporting was noted for SEA, EMR, and WPR as the second, third, and most important issue, respectively. Lack of commonly accepted standards was noted as being very important for AFR and EUR, while the absence of relevant health-state preference data was more of an issue for PAH and inappropriate choice of comparator was noted for EUR. (Table 5)

Table 5: Comparison of top 3 priority technical issues in the different regions

SEA Ranking		AFR Ranking		PAH Ranking		EUR Ranking		EMR Ranking		WPR Ranking	
1	Lack of high quality local clinical data, where such data are critical to the decision	1	A lack of commonly accepted standards for economic evaluation that's relevant to the LMIC for which the analysis is undertaken	1	Lack of high quality local clinical data, where such data are critical to the decision	1	A lack of commonly accepted standards for economic evaluation that's relevant to the LMIC for which the analysis is undertaken	1	Lack of high quality local clinical data, where such data are critical to the decision	1	Poor Reporting
2	Poor Reporting	2	Lack of high quality local clinical data, where such data are critical to the decision	2	Insufficient data to conduct study from chosen perspective	2	Insufficient data to conduct study from chosen perspective	2	Insufficient data to conduct study from chosen perspective	2	Lack of high quality local clinical data, where such data are critical to the decision
3	Insufficient data to conduct study from chosen perspective	3	Insufficient data to conduct study from chosen perspective	3	Absence of locally-relevant health state preference data suitable for estimating QALYs or DALYs	3	Inappropriate choice of comparator (s)	3	Poor Reporting	3	A lack of commonly accepted standards for economic evaluation that's relevant to the LMIC for which the analysis is undertaken

In terms of the priority context-specific issues, exclusion of economic evaluation from the decision making process is an issue for all settings, particularly in SEA, AFR, EUR, and EMR. It is the second most important issue in WPR and the third in PAH. The second most important issue is the lack of funding for the research, which, while considered the third most important issue in SEA, AFR, EUR, and WPR and the most important issue in PAH, is present in all settings except for EMR. The third most common issue is the limited capacity, which is an issue in AFR, PAH, EMR, and WPR. Lastly, misunderstandings and weaknesses in communication between researchers and relevant stakeholders has been cited as another important challenge. (Table 6)

Table 6: Comparison of top 3 priority context-specific issues in the different regions

SEA Ranking		AFR Ranking		PAH Ranking		EUR Ranking		EMR Ranking		WPR Ranking	
1	Economic evaluations not included as a part of the decision-making process	1	Economic evaluations not included as a part of the decision-making process	1	Lack of funding for the necessary research	1	Economic evaluations not included as a part of the decision-making process	1	Economic evaluations not included as a part of the decision-making process	1	Limited local capacity to conduct or contextualize research
2	Misunderstandings and communications weaknesses between researchers, academia and end users of the evidence	2	Limited local capacity to conduct or contextualize research	2	Limited local capacity to conduct or contextualize research	2	Misunderstandings and communications weaknesses between researchers, academia and end users of the evidence	2	Limited local capacity to conduct or contextualize research	2	Economic evaluations not included as a part of the decision-making process
3	Lack of funding for the necessary research	3	Lack of funding for the necessary research	3	Economic evaluations not included as a part of the decision-making process	3	Lack of funding for the necessary research	3	Misunderstandings and communications weaknesses between researchers, academia and end users of the evidence	3	Lack of funding for the necessary research

## Survey Groups

In addition to disaggregation by geographical areas, responses were also analysed in terms of specific survey groups.

In terms of years of experience, there was no difference in the ranking of context specific issues; however, for the technical issues, instead of the lack of local clinical data, those who were more experienced believed that poor reporting was more of an issue. Those who were more experienced were also more concerned about conducting sensitivity analysis, which came in the third place in their ranking of technical issues. (Table 7 and 8)

Tables 7 and 8: Priority issues by years of experience

Less than 5 years of Experience (Ranking)	Technical Issue	Context-Specific Issue
1	Lack of high quality local clinical data, where such data are critical to the decision	Economic evaluations not included as a part of the decision-making process
2	Insufficient data to conduct study from chosen perspective	Limited local capacity to conduct or contextualize research
3	Absence of locally-relevant health state preference data suitable for estimating QALYs or DALYs	Lack of funding for the necessary research

More than 5 years of Experience (Ranking)	Technical Issue	Context-Specific Issue
1	Poor Reporting: <ul style="list-style-type: none"><li>• Perspective of analysis not stated</li><li>• Lack of details of the target population or sub-populations relating to the interventions being evaluated</li><li>• Lack of detail on the methods used to derive the measure of benefit</li><li>• Lack of details to enable checking of data sources for benefits / effectiveness</li><li>• Lack of details to enable checking of data sources for costs</li><li>• No details of the price year used as the basis of the cost analysis</li><li>• Methodology not presented in a clear and reproducible manner</li></ul>	Economic evaluations not included as a part of the decision-making process
2	Lack of high quality local clinical data, where such data are critical to the decision	Limited local capacity to conduct or contextualize research
3	No, or inappropriate, sensitivity analysis	Lack of funding for the necessary research

The results were also analysed according to the responses from academics and public health institute respondents, since they were the highest in number of respondents of the different affiliations.

For academics, the most important technical issue is lack of local clinical data, while for public health institutes, it is poor reporting. Both these groups report the non-inclusion of economic evaluation to

the decision making process as being a significant issue for the use of economic evaluation in healthcare policy making in developing countries. (Table 9 and 10)

Tables 9 and 10: Priority Issues by Affiliation

<b>Academics (Ranking)</b>	<b>Technical Issues</b>	<b>Context-Specific Issues</b>
1	Lack of high quality local clinical data, where such data are critical to the decision	Economic evaluations not included as a part of the decision-making process
2	Insufficient data to conduct study from chosen perspective	Limited local capacity to conduct or contextualize research
3	Absence of locally-relevant health state preference data suitable for estimating QALYs or DALYs	Lack of funding for the necessary research

<b>Public Health Institute Employees (Ranking)</b>	<b>Technical Issues</b>	<b>Context-Specific Issues</b>
1	Poor Reporting: <ul style="list-style-type: none"> <li>• Perspective of analysis not stated</li> <li>• Lack of details of the target population or sub-populations relating to the interventions being evaluated</li> <li>• Lack of detail on the methods used to derive the measure of benefit</li> <li>• Lack of details to enable checking of data sources for benefits / effectiveness</li> <li>• Lack of details to enable checking of data sources for costs</li> <li>• No details of the price year used as the basis of the cost analysis</li> <li>• Methodology not presented in a clear and reproducible manner</li> </ul>	Economic evaluations not included as a part of the decision-making process
2	Insufficient data to conduct study from chosen perspective	Limited local capacity to conduct or contextualize research
3	Absence of locally-relevant health state preference data suitable for estimating QALYs or DALYs	Lack of funding for the necessary research

### **Context-specific vs. technical issues**

There are 66% of respondents that report context-specific issues as being more of an impediment to economic evaluation compared to technical issues (34%). (Figure 11)

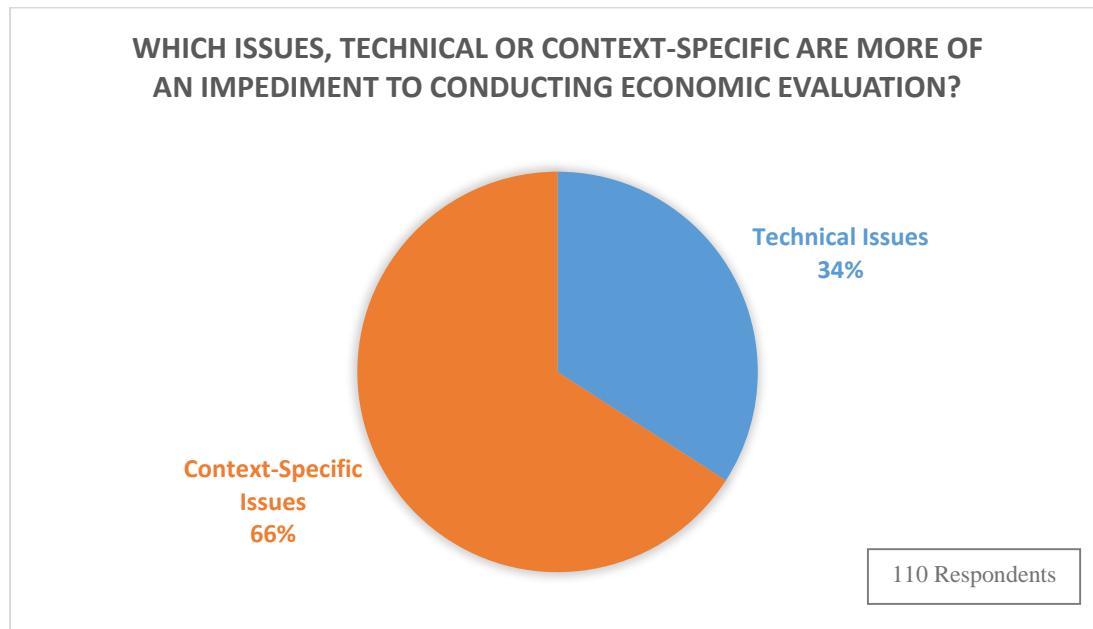


Figure 11: Respondents' responses on which issue is more important, technical or context-specific

## Proposed solutions

Respondents proposed some solutions in order to overcome technical and context-specific issues. The solutions were grouped together and duplicates were removed.

Table 11: Respondent-proposed solutions

Technical solutions	Context-specific solutions
<p>Construct a database for collation of all data and information needed in the conduct of economic evaluations, i.e. cost data and clinical data, through the compilation or linking together of data that already exists in the health systems.</p> <p>Develop utility or disutility weights for LMICs locally and/or by region.</p> <p>Develop methods to measure non-health outcomes, e.g. restored productivity.</p> <p>Develop standard methodological and reporting guidelines for economic evaluations that are acceptable (i.e. understandable and perceived useful) for decision makers and stakeholders in the country.</p> <p>Support the conduct of local clinical studies.</p> <p>Link and network with other researchers working in developing countries for knowledge and research sharing.</p> <p>Conduct research to estimate cost-effectiveness threshold</p>	<p>Engage all relevant stakeholders in performing economic evaluations and facilitate more interaction between and among different stakeholders.</p> <p>Build capacity both in terms of quantity and quality for but not limited to economic evaluations. The capacity in focus may be expanded to other HTA studies and its concerns, e.g. safety, effectiveness, equity, etc.</p> <p>Apply other types of study to policy-making in addition to economic evaluations. Develop a more deliberative process as economic evaluations are not the final answer and research with broader scope, e.g. macro HTA, which is assessment of the efficiency at health care system level  <a href="http://www.ispor.org/conferences/Mexico0911/presentations/PhRMAsymposium_3LA.pdf">[http://www.ispor.org/conferences/Mexico0911/presentations/PhRMAsymposium_3LA.pdf]</a> MCDA, have to be considered.</p>

## Other related studies

In reviewing the literature, of the 25 studies included in the preparatory work for the questionnaire [5-10, 29, 11-15, 30, 16-22, 24-27], the majority of studies exploring methodological issues revolve around disease-specific economic evaluations from low- and middle-income countries, mainly for sexually transmitted disease interventions (6 studies), non-communicable diseases interventions (5 studies), and vaccinations (2 studies). Those that assessed economic evaluations focused primarily on country-specific studies (7 studies, though one overlaps with a disease-specific issue). The rest are either regional or provide a general review of the methodological issues involved in economic evaluations.

Other studies that are similar in nature to this one were cited by the respondents as well, though most seem to be of the same nature as those found during the literature review. One respondent reported that the ISPOR Africa Network is embarking on a survey within Africa to look at policy, capacity and constraints in conducting economic evaluations among the African ISPOR members (South Africa, Ghana, Uganda, Algeria, Egypt, and Morocco) in conducting economic evaluations. One respondent shared information on a study being conducted by Inge van der Putten in the Maastricht University ([https://maastrichtuniversity.eu.qualtrics.com/jfe/form/SV\\_6fJ1Yf39KJKjqOF](https://maastrichtuniversity.eu.qualtrics.com/jfe/form/SV_6fJ1Yf39KJKjqOF)) and was found to be more focussed on the impacts of vaccines. Another respondent mentioned that the International Decision Support Initiative (iDSI), also conducted a research methods survey in 2014. The RAHEE conducted in Europe is another example, though this study's aims are to understand the top disease burdens in the continent and to prioritize them for subsequent research.

A relevant study conducted was Longworth et al's review of research priorities for the National Institute for Health and Care and Excellence (NICE) [23]. This study's primary aim was to create a priority list of topics for methods research to support the decision-making processes in NICE, which is similar to the study being conducted, though it is much more focused in scope. A focused literature review, interviews, an email survey, a workshop and a web-based feedback exercise were the primary methods used to gather information. Members of the NICE secretariat and its advisory bodies, representatives from academia, industry, and other organizations working closely with NICE participated. Though the Web exercise was open to all, it was sent primarily to the above groups. The following priorities emerged from the group that works closely with NICE: methodology for indirect and mixed treatment comparisons; synthesis of qualitative evidence; research relating to the use of quality-adjusted life years (QALYs) in decision making; methods and empirical research for establishing the cost-effectiveness threshold; and determining how data on the uncertainty of effectiveness and cost-effectiveness data should be taken into account in the decision-making process. The following priorities emerged from the broadest group of respondents: methods for extrapolating beyond evidence observed in trials, methods for capturing benefits not included in the QALY and methods to assess when technologies should be recommended in the context of further evidence gathering. Two limitations identified by the authors are the short timeframe in which the study was conducted as well as the low response rate from international agencies. While these limitations suggest the findings may not be generalised to other settings, the targeted participants in the study ensures that the results are relevant to policy.

Drummond and Marshall report results of a forum to understand the priority methodological research in the evaluation of health technologies conducted in Canada [31]. This forum included representatives from the Canadian Agency for Drugs and Technologies in Health (CADTH), NICE, Alberta Health and Wellness and several industry partners (Pfizer, Merck, Eli Lilly, Astra Zeneca and Glaxo Smith Kline) and divided the analysis into policy and methodological issues. For policy issues, the results are the following: emphasizing the rigour as well as the timeliness of the results of HTA studies, working not only on assessment but also management of healthcare, studying the gradual and step-wise process of technology introduction and use. The results for methodological issues were:

data quality and the development of national costing panels, incorporation of the use of routine patient reported outcomes, incorporation of multi-criteria decision frameworks into economic evaluation and policy-making, mitigating against methodological bias in economic evaluations, and incorporating a broader and societal perspective in the economic evaluation. Given that the results included perspectives from HTA agencies and industry, this report is valuable in terms of informing policy making. In discussions based on international experiences, they also highlighted the importance of methodological research being useful for policy-making, involvement of decision makers to ensure that the research fits their needs, and the translation of these ideas into researchable questions.

## Stakeholder Consultation

The results were generally said to represent the situation in LMICs. However, some of the major points raised revolved around the complexity and intertwining aspect of context-specific issues and technical issues, particularly in terms of the lack of good quality data. For instance, lack of good clinical data may be due to lack of investment in information systems and is therefore tied to the funding issue, which falls under context-specific issues in this study. Another example is that while there may be good guidelines on reporting, lack of capacity or knowledge of these may prevent researchers from using them; as such, the existing premise and even title of the project may disregard the research and work that currently exists. However, though this may be the case, such issues can still be addressed with methodological solutions, such as exploring methods that LMICs may be able to conduct better research while accounting for lack of data and/or funding (e.g. more cost-friendly but still robust implementation research).

Another point is the usefulness of clumping the data and generalizability issues together. This affects the study's transferability and also the applicability of the information to other settings. With this in mind given the use of data from other countries, some of the data issues may be addressed. In Chile and other Latin American countries, while it is assumed that LMICs do not conduct RCTs, they may do so out of a necessity to conduct clinical trials. However, clinical practices change and it may not be viable to transfer data from other countries. Currently, these countries transfer data from others for use in their studies. Nevertheless, language issues can be a concern, as countries may find it difficult to use information from other countries where the studies are only available in the local language(s). This also results in variability in standards and research practices in the region. Further, clinical definitions in different countries may be different and irrelevant to the local context to which it is being transferred.

Country priority setting practices were also highlighted as a possible factor affecting the research. Some countries that use economic evaluation research may use them during the decision making process along with other pieces of evidence, but the presence of the evidence does not necessarily lead to a decision. In addition, the studies in Latin America, for example, are not always published, leading to variation in reporting that differs from international guidelines. Though this may be true, other methodological solutions can address them, such as the use of guidelines or conducting research that accounts for the health system capacity and situation. Another point is that several actors may affect the development of a healthcare system, consequently influencing the data availability and the information system management. In addition, while there is intertwining between technical and context-specific issues, this study was geared towards addressing methodological issues that could be explored in future research within the context of the limitations faced by LMICs. The results of the study will lead to an improvement in the use of evidence.

In addition to the solutions cited in this study, some participants made the following suggestions: have practical examples for use of evidence in developing countries based on guidelines; develop a medium tool that can be used to transfer data (e.g. costs, utility, etc.); and have regional HTA agencies conduct due diligence on data transferability in their regions, which can be shown in the database or updated in other existing ones.

## Discussion

Across all settings, the study shows that the most important technical issue is the lack of quality local clinical data, poor reporting, and insufficient cost data to conduct the analysis from the chosen perspective. Lack of clinical data, the most important issue, is characteristic of undeveloped health systems in resource-limited countries. Challenges already exist in provision of healthcare, which exacerbate difficulties in coordinating data collection and management in the public and private sectors. Due to these gaps, conducting economic evaluation may depend on limited data and result in over representativeness or over-generalization of the results. The second most important issue is poor reporting, which may primarily be due to a lack of coordination as well as process and guidelines on a national level for the studies being conducted. Similar to the first issue, the third most important barrier is insufficient cost data to conduct the analysis from the chosen perspective, which is tied to all the other two issues.

The study also examined the differences in important issues between the different regions as well as specific survey groups. Interestingly, for respondents that have worked in Africa and developing countries in Europe, the most important issue is the lack of commonly accepted standards for economic evaluation; a probable explanation is the significant presence of donors that conduct a variety of economic evaluations through various programs. These programs may have overlapping goals or could be combined as part of a single program; research conducted could benefit from coordination between them. In West Pacific, the most important issue was poor reporting, which may result from several studies being conducted but are not reported in a standardized manner. Respondents with less experience state that lack of data is the most important issue, while those with more experience state that it is poor reporting. These issues in economic evaluation may therefore be about lack of a standard reporting guideline. Academics report that lack of data is the most important issue, while public health institute employees state that it is poor reporting. Understandably, academics are concerned with the robustness of the results, while those that work directly with governments believe that standardizing reporting and communicating results appropriately may be paramount.

The findings of rankings and solutions on the issues from the survey were triangulated with some other proposed solutions from other expert opinion in order to address all the top priority issues. The issues and solutions were then linked and potential research questions for studies that aim to improve quality of economic evaluations were listed in companion with the hypotheses that underlined those research questions (please see Appendix 2 for Table 13).

Many respondents proposed a solution to develop methodological and reporting guidelines for the conduct of economic evaluations which would help standardize the conduct and the report of the studies. On the other hand, there have been widely available guidelines developed by various groups of people. For example, for reporting, there exists the Consolidated Health Economic Evaluation Reporting (CHEER) statement [32], and for the methodology or the conduct of the study, there is the WHO Guide to Cost-Effectiveness Analysis [33]. However, the issue of lack of such standard is still a high priority which indicates that these guidelines have not been used. This may be caused either by lack of awareness of the existence of the guidelines or the guidelines from other contexts being viewed as unacceptable; the guidelines have to be understandable and perceived useful, in LMIC context. As a result, guidelines may need to be acceptable for stakeholders in each country, either through adopting international guidelines or developing country- or context-specific guidelines that are suitable for the application in LMIC settings. Considering variation of concerns e.g. political or cultural, in different contexts, the latter may result in better accepted guidelines. International guidelines can be used as a starting point for such guidelines development, of which the process should be participatory, bringing stakeholders and various groups of expert together to ensure the development of capacity alongside guidelines development. A perfect example of this kind of guidelines that can be

further built upon is the Gates Reference Case developed by iDSI and launched by the Bill and Melinda Gates Foundation [34]. The reference case was developed with the specific focus on its feasibility to be applied in LMICs. It is principle-based and recommends some methodological specifications, i.e. it offers an aid to thinking on practices that need to be introduced but allows for researchers to make decisions on the details of the practice so that it is compatible with the country and the needs of policy-makers. For example, for health outcome measure, in principle, the reference case recommends that the measure is appropriate for the decision problem, captures all the consequences, and is generalizable between health states. As a methodological specification, the use of Disability-Adjusted Life Years (DALYs) is recommended. However, researchers may vary the methods of DALY calculation, e.g. age-weighting or life tables, to reflect views of stakeholders in their countries. To foster the use of guidelines including the reference case, factors affecting the acceptability of the guidelines among stakeholders should be explored.

The lack of high quality local clinical data might be caused by the lack of randomized-controlled trials (RCTs) which are considered a gold standard. For settings where RCTs were conducted, the clinical practice adopted in those trials may be incompatible with local clinical practice elsewhere. The conduct of RCTs is also costly and unaffordable for governments. Although clinical data or treatment effect of an intervention is considered transferable [35] and those from high-income settings should be applicable to the LMIC contexts, many stakeholders doubt this. More importantly, clinical practice in LMICs sometimes differs from that in high-income settings, making it impossible to apply clinical data from high-income settings. For example, while biologic agents are used for the treatment of rheumatoid arthritis as a second or third line drug in high-income settings, it is, however, the fourth line treatment in Thailand. As a result, the characteristics of patients who meet the criteria are different and results of studies in high-income settings are not applicable. Solutions to this can be through increasing number of high quality, pragmatic RCTs [36] and experimental studies that are conducted using local clinical practices, by or selecting studies that are applicable to LMIC contexts or by developing a non-RCT approach that is acceptable to estimate clinical benefits of health interventions. In addition, other types of implementation research [37] that are comparable to RCTs may be developed. These would help reduce the cost of achieving clinical data that is suitable for the setting. The issue may also be extended to the lack of high quality epidemiological or baseline clinical data. Developing a registry to store such data, probably at national level, with a quality assurance process might help overcome the issue. However, the collection of these types of data tends to be costly and requires human capacity. The feasibility of constructing such a registry should be explored. There is also the case where there is no standard clinical practice in some LMICs so data collection on the standard practice would also be useful.

Many respondents were concerned with the utility and disutility weights which should reflect reality in the country. Although there is a set of global quality of life (disability) scores made widely available by the WHO [38], quality of life tends to differ from one country to another and sometimes even within the same countries where there is a high level of heterogeneity in terms of religion, lifestyle, country infrastructure and geography. Most of LMICs do not have their own tariff for calculating utility or disutility scores and developing one would result in considerably high costs. Developing a tool to examine whether it is possible to transfer utility/disutility scores from a setting to another would help overcome this. Another possible alternative is to develop a set of regional utility/disutility scores. Although there can be differences among countries in the same region, the regional utility/disutility score would better reflect the country context when compared to the global one.

The use of a threshold has been controversial even in high-income countries and definitely in LMICs. Although WHO announced a guide to threshold (1-3 time gross domestic product (GDP) per capita), it has been found that the guide to threshold level proposed might not reflect the country context [39-44]. Therefore, another guide to estimate thresholds in each country should be developed. On the other hand, policy-makers can also choose to rely on other types of evidence on financial impact that

does not require a threshold, e.g. budget impact analysis, or adopt other approach to prioritize, e.g. league table, instead.

Another issue of concern is the lack of cost data which limits the ability to conduct studies from the chosen perspective. This can be overcome by the construction of a database for such data and other non-health related outcomes. In Thailand, there is a database for standard cost lists for health technology assessment [45], which is an online database developed by HITAP in collaboration with Faculty of Pharmacy, Mahidol University with the aim to strengthen HTA infrastructure. The database provides estimates of cost items including direct medical costs and direct non-medical costs, e.g. travel cost for hospital and primary care units. In order to derive each cost item, a significant volume of data was required and there were many difficulties. The development therefore could be expensive, time-consuming and easily misinterpreted. If there are tools or guidelines to help overcome these problems in conducting a costing study, it would facilitate the conduct of economic evaluations and also standardize the cost data collected.

Some general issues arising from the results is the transferability or generalisability of evidence (especially those coming from high-income contexts) and the lack of local data for costs, clinical information, outcome measures and others. For the first issue, several studies have explored whether certain studies can be transferable to other settings (e.g. Welte for economic evaluation [46]). The importance of clear reporting, another issue of concern for respondents, was also cited as good practice for transparency that would help with determining the transferability of studies [45]. For the second issue on lack of data, some concerns are tied to systemic issues, particularly lack of commitment to use evidence in decision making, consequently leading to insufficient investment in data systems and routine data collection. A solution to the issue maybe to form groups of context which are considered to be similar enough that the information can be shared and transfer. With the collaboration, less investment will be needed for the member of the group [47]. If this investment issue is addressed, this could potentially solve issues not only on insufficient data but also information on local clinical practices. While investing in these systems could prove expensive as mentioned before, HTA organizations such as NICE in the UK and HITAP in Thailand began conducting research even when information was scarce (e.g. lack of unit costs in the UK at the time of NICE's establishment in 1999).

For context-specific issues, the lack of integration of economic evaluation evidence into the decision-making process was accorded the highest priority. Although it can be argued that researchers should produce high-quality research regardless of the demand from policy-makers, the absence of such demand results in the lack of incentives for researchers to perform better as well as the political support for the development of relevant infrastructure. The buy-in can be improved through awareness raising and identifying the barriers that hinder such use. If acceptability on economic evaluation is low, a possible option is to employ other approaches for health priority-setting, such as MCDA. Regarding limited local capacity to generate contextualized research, improvements can be made by incentivizing and training researchers to work in this field and ensure that they have the highest possible performance. To solve the issue on the lack of funding, it should be made clear how not investing in research may affect the countries. For example, how much opportunity costs are foregone. Policy-makers' willingness-to-pay for the research should also be examined as information for further planning in the contexts. In general, the context-specific issues can also be considered as part of broader capacity issues, e.g. capacity to conduct, use, commission research and others, including the capacity to fund the development and continued use of good evidence in the decision-making process [38].

The stakeholder consultation showed that the experts and policy implementers viewed the results as accurate, although a major point was the intertwining aspect of context-specific issues and technical issues, particularly in terms of the lack of good quality data. Inappropriateness of the transferability

of data due to language barriers across and within countries as well as differences in the clinical context of countries could impede the development of quality data. On the other hand, context-specific issues can be addressed by finding solutions that would fit the health system or resources of the country. The study separated technical and context-specific issues in order to address methodological issues that could be explored in future research within the context of the limitations of LMICs.

These findings are promising; however, this working paper is not without limitations, primarily the low response rate from certain regions. In spite of sending the results to various networks, lack of access to email databases meant that the survey reminder and compliance relied on a secondary party and not the researchers. This also affected the response rate since duplications could not be removed. The study has considerably more respondents from the Asia and the Pacific regions because the researchers have access to these network databases. In addition, there is no network for potential respondents in the East Mediterranean, which resulted in this region having the lowest number of respondents. Finally, the review of literature discussing methodological issues included those of both LMICs and HICs and the framework for reviewing these economic evaluations in LMICs is from the CRD, which is based on HIC methods and experts. The issues identified are therefore not exclusive to LMICs context. In other words, the “fishing bait” in looking at methodological issues is the same in LMICs and HICs, then the same type of results or “fish” may be found. However, there may be a different result for another, more specific methodology. This suggests that more attempt may need to be made for further studies on the methodological issues in LMICs. For example, identifying methodological issues by conducting an interview with scholars in LMICs first to get a better understanding of their methodological problems and construct a survey based on the findings of the interview.

In spite of these limitations, the results of this study give a preliminary understanding of the issues faced by researchers in developing countries. The final results after will be inputted into the iDSI program of future work on methodological development in 2016-2019. The results will therefore ultimately assist researchers in providing robust evidence to policy-makers in the decision making process for health resource allocation. To inform the global community since to ensure all the gaps are filled, combined effort is crucial. As such, the research results will also be used to inform the creation of a database that will function as a comprehensive web-based knowledge sharing platform that addresses methodological issues regarding policy relevant research. The site will showcase the results of this research, but also allow registered users to examine in detail the issues according to geography, respondent demography, and other relevant factors as well as access and contribute to the referenced research papers. In the future, the database may allow registered users not only to take the survey and update the results in real time, but also include their own research questions to those detailed in the website and determine immediate solutions to their methodological problems through the various functions of the database.

## Database Creation and Next Steps

The database is designed as a global public good dedicated towards helping LMIC academics, researchers and economic evaluation practitioners worldwide to conduct high quality, policy relevant healthcare research. The database will explore the issues in the conduct and the use of evidence, offer potential solutions to the issues and inform future research questions to address these issues. It will also provide various alternatives to solve specific methodological difficulties that researchers may encounter in the conduct of their studies. In addition to information from the stakeholder consultation, the database features were also discussed during the iDSI board meeting at the Prince Mahidol Award Conference 2016 and presented below, along with recommendations sent via personal communication.

However, the research team foresees that in addition to filling the gaps through research which will require substantial amount of time, providing users with 'immediate solutions' that could be used to tackle methodological difficulties they are currently facing is just as important. This component is envisaged to be a part of the Theory of Change of Methodological Research Development outlined below (Figure 12). The prioritization of methodological problems and finding solutions to these issues will lead to methodological research that will yield improved tools for the conduct of economic evaluations. The quality and usability of economic evaluations will be boosted as a result and the decision-making informed by this evidence will also be better. This could potentially call for sustainable production of evidence and even higher quality and usable evidence. The availability of immediate advice from current and existing research for researchers' use to overcome methodological difficulties is at the heart of the database's function.

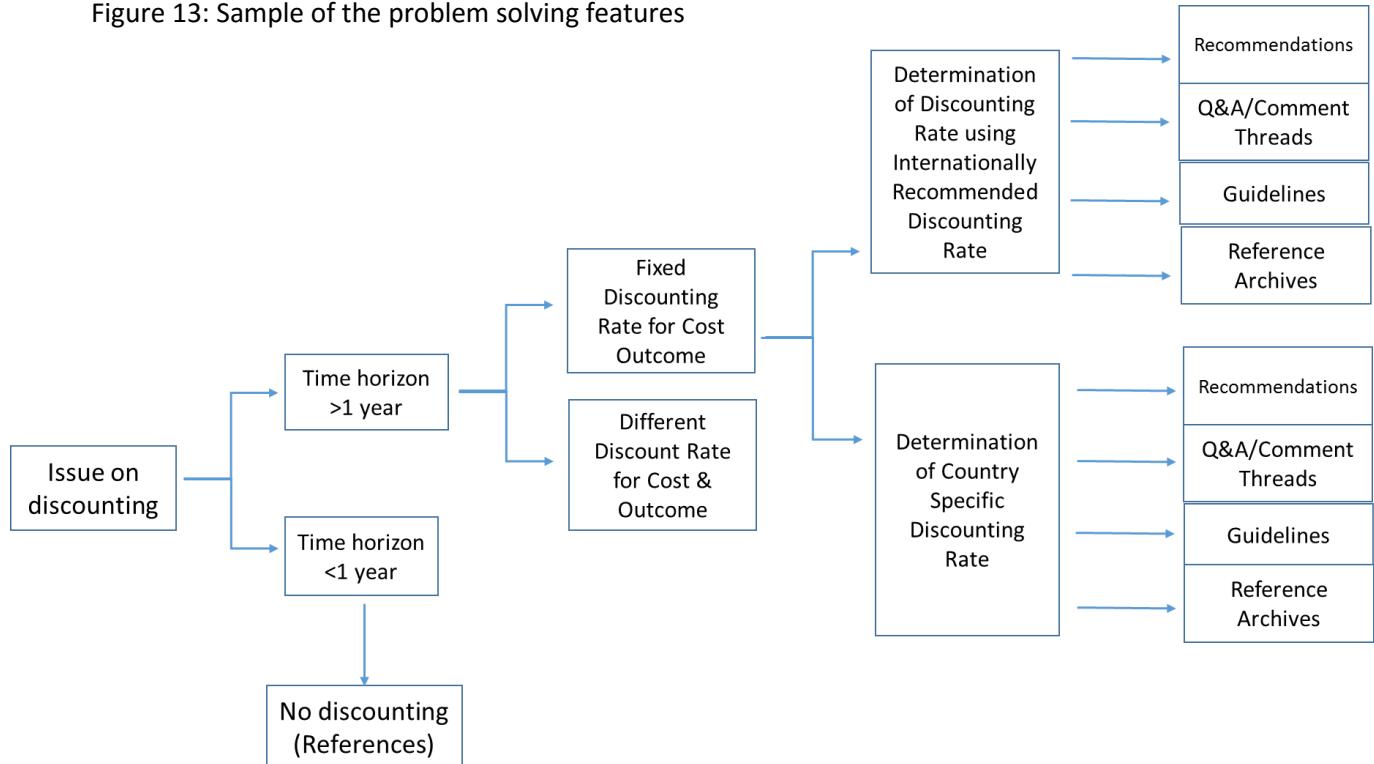
Figure 12: Immediate advice and Theory of Change of the database



The features to be included are as follows:

- ❖ Problem solving: provide immediate solution in the form of mind-map linking methodological difficulties to possible solutions based on literature and experts' experience. (Figure 13)
  - Exploring established areas: outline recommendations to tackle the difficulties based on theory and consensus for the issues of which the standard practice has been agreed upon from guidelines or textbooks. Statistics on methodological characteristics of existing economic evaluation studies will also be provided based on the data retrieved from ***Global Health Cost Effectiveness Analysis Registry*** developed by Tufts University.
  - Comparing guidelines: head to head comparison on the issue of interest and usability between selected economic evaluation guidelines available at international, regional and national levels for high-income and low- and middle-income countries. Potential guidelines for the first phase of development are iDSI Reference Case, ISPOR Taskforce's Good Research Practice for Cost-Effectiveness Analysis, WHO Guide to Cost-Effectiveness Analysis, EUNEHTA, NICE Guidelines and Thai national guidelines.
  - Q&A/Comment threads: Offer researchers globally a platform for open discussion, comment threading and assistance to other researchers. Users can upload their questions regarding the conduct of economic evaluations. The answers to the questions will be made available within 7 days by a group of experts. There will be a moderator who will pass relevant questions to the expert on the related issue. The answers are contestable. Should there be alternate opinions that differ from the answer provided by the expert, the opinions will be displayed together with the original. Keywords tag will be applied to facilitate questions and answers searches.
  - Reference Archives: Collections of links to publications focusing on issues are provided as a tool to further the understanding of users. The archive will be updated regularly based on reviews of selected journals specializing in economic evaluation. Users, e.g. authors of publications, can also upload related research which will be reviewed for its relevance to the issues before its availability online as a part of the collections.

Figure 13: Sample of the problem solving features



- ❖ Filling the methodological gaps through research: outline priority issues in LMICs derived from the survey with relevant solutions proposed by the respondents. Hypotheses underlying each solution will be provided followed by research questions that build on the hypotheses. Reference to publication focusing on the solutions and hypotheses will also be provided.
  - Visualization options: options available for user to visualize information in a tabular form or a mind map form. Mind maps outline a central concept around an issue or a solution and visually organize research information and ideas.
  - Global and regional information: priority issues in different regions differ so they are displayed separately and also as a whole for global priority issues.
  - Filter by respondent demography: the information can be filtered by demographic characteristics of the respondents, e.g. affiliation, years of experience.
  - Interactive Platform: users can propose relevant solutions to the priority issues as well as related research questions and publications. The proposal will be updated to the website upon moderator's review for their relevance to the issues.
  - Real-time database survey: users can take the survey which will be available on the database. Results from the real-time survey will be displayed separately from the original to compare the primary results to the most updated results. Results are automatically updated upon the response submission. Every 2 years, the survey will undergo major revision based on responses received from previous surveys.

The primary users will be researchers, academics, public health institutes, and others that conduct policy research. Users will be able to choose from a variety of solutions that will be relevant to their context. However, the website will begin with 5-8 priority issues based on the information gathered from the survey and expand over time to others (e.g. thresholds). Possibilities of linking the database with others in existence (such as the cost-effectiveness analysis registry <https://research.tufts-nemc.org/clear4/>) are currently being explored. The researchers are considering collaborations with various research agencies, the WHO, and HTA networks such as HTAsiaLink and iDSI to assist as experts in the immediate solutions feature.

The best outcome is for the website to become a changing, living document, which provides up-to-date and relevant information. Once the website has been built and its usability is proven over time, it will be linked with other capacity-building activities of various networks and agencies to ensure that the project's goals are met.

## Acknowledgements

This project was conducted through the International Decision Support Initiative (iDSI, [www.idshealth.org<http://www.idshealth.org>](http://www.idshealth.org)), a global initiative to support decision makers in priority-setting for universal health coverage. iDSI receives funding support from Bill & Melinda Gates Foundation, the UK Department for International Development, and the Rockefeller Foundation.

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## Appendix 1

A number of other analyses were conducted to further outline the characteristics of the survey respondents

Ranking (no.)	Country	Response Count
1	TH - Thailand	15
2	GB - United Kingdom	13
3	MY - Malaysia	10
4	US - United States	10
5	BR - Brazil	6
6	CN - China	6
7	PH - Philippines	5
8	IN - India	4
9	ZA - South Africa	4
10	ID - Indonesia	3

Table 12: Number of Country Respondents by rank

The highest number of respondents was from Thailand, then the United Kingdom, Malaysia, the United States, and Brazil, and China.

## Appendix 2

Table 13: Potential solutions and example of research questions to overcome the issues that limit the use of economic evaluations

Problems	Issues in the Use	Stakeholders / Affected Parties	Relevant Solution	Hypothesis	Example research Question(s)
<b>Technical issues</b>					
Generalizability not discussed	Difficulties in the application of the study result in other contexts	Policy-makers and researchers from other contexts	Standard methodological and reporting guidelines for economic evaluations that are acceptable (i.e. understandable and perceived useful) for decision makers and stakeholders in the country.	1. The methodological guidelines involve politics and that it may be difficult for national authority to approve international guidelines for its use in policy decisions.	1. Is it acceptable for country decision makers and stakeholders to use international guidelines as a recommendation for country study?
Equity and/or gender implications not considered	Difficulties in considering the evidence for decision making	Policy-makers in the context			
Clinical data not based on systematic review; or primary clinical data not compared with similar studies done elsewhere	Limited power of the study	Policy-makers			

<b>Problems</b>	<b>Issues in the Use</b>	<b>Stakeholders / Affected Parties</b>	<b>Relevant Solution</b>	<b>Hypothesis</b>	<b>Example research Question(s)</b>
Inappropriate choice of comparator (s)	Misleading recommendations	Policy-makers		2. The national guidelines available may not be much different from the international standards and national guidelines from other countries.	2. Are there similarities and differences of international and national guidelines currently available?  3. What are the experiences and approaches used to develop national guidelines that are acceptable for decision makers and stakeholders in the country?
A lack of commonly accepted standards for economic evaluation that's relevant to the LMIC for which the analysis is undertaken	Difficulties to compare across studies and difficulties in making decision based on the results.	Policy-makers			
Poor Reporting	Limited utilization since the relevance to the context is limited	Audience of the research e.g. policy makers, other researchers			

<b>Problems</b>	<b>Issues in the Use</b>	<b>Stakeholders / Affected Parties</b>	<b>Relevant Solution</b>	<b>Hypothesis</b>	<b>Example research Question(s)</b>
Lack of high quality local clinical data, where such data are critical to the decision		Researchers, policy-makers in the context	<p>1. Having more high quality clinical studies (RCTs and experimental studies) conducted in LMICs using local clinical standard.</p> <p>2. Using non-RCT approach to estimate clinical benefit of health intervention in LMICs.</p>	<p>1. Clinical information is generalisable across settings.</p> <p>2. RCTs is the gold standard for the evaluation of clinical benefit of health interventions.</p> <p>3. RCTs conducted in LMICs are mostly funded by industries and use clinical practice standard of HICs because they aim for supporting registration and marketing in HICs.</p> <p>4. RCTs and experimental studies are too expensive and infeasible to be funded by government in LMICs.</p>	<p>1. Is the clinical data really generalizable/transferable across settings?</p> <p>2. Is efficacy information relevant and useful for HTA in LMICs?</p> <p>3. How to develop an approach, e.g. checklist, to assess the relevance and robustness of data from clinical studies to local practice standard?</p> <p>4. Is it possible to develop a study design (including data collection and analysis) that is feasible, affordable and robust for the use in LMICs?</p>

<b>Problems</b>	<b>Issues in the Use</b>	<b>Stakeholders / Affected Parties</b>	<b>Relevant Solution</b>	<b>Hypothesis</b>	<b>Example research Question(s)</b>
				5. It is possible to develop affordable implementation research in LMICs to estimate clinical benefit of health interventions and that are comparable to RCTs	5. Is it possible to develop analytical approach for real world data analysis that is comparable to RCTs
				3. Develop a tool or guidelines for developing registry for baseline clinical data and database for standard practice in the country (including data collection and analysis of such data)	6. Though the process may require high resources both in terms of cost and human capacity, baseline clinical data registry and database for standard practice help improve quality of such data and facilitate the conduct of economic evaluations.

<b>Problems</b>	<b>Issues in the Use</b>	<b>Stakeholders / Affected Parties</b>	<b>Relevant Solution</b>	<b>Hypothesis</b>	<b>Example research Question(s)</b>
Absence of locally-relevant health state preference data suitable for estimating QALYs or DALYs		Researchers, policy-makers in the context	Having regional or national utility scores for the use in different settings.	Global utility scores (e.g. disability weight) are unacceptable for use at national level, especially in LMICs, because decision-makers perceive different utilities or disability weights for the same health condition across jurisdictions	<p>1. Is it more appropriate to use regional- or sub-regional-derived utility scores or disability weights for economic evaluations?</p> <p>2. Taking into account the social, economic and health system contexts, is it feasible to develop an approach to translate utility scores or disability weights derived from one setting to another?</p>
No budget constraints or thresholds considered	No guidance on the cut-off point of cost-effectiveness	Policy-makers in the context	Identifying standardized methods to identify the threshold that reflects the country context	1. WHO threshold, which is commonly used for countries that have just started conducting economic evaluations, does not appropriately reflect country-specific contexts	1. How to develop an approach for deriving a threshold that is relevant to the country, acceptable and useful for policy-decision?

Problems	Issues in the Use	Stakeholders / Affected Parties	Relevant Solution	Hypothesis	Example research Question(s)
				2. The decision making process may also require other information that not necessary needs threshold (e.g. budget impact analysis)	2. Is a threshold necessary for policy-making in LMICs?
Insufficient data to conduct study from chosen perspective	Inability to respond to a question from stakeholders	Researchers	Develop a tool or guidelines for developing standard cost list (including data collection and analysis of cost data)	Though the process can be complicated and complex, standard cost list help facilitate the conduct of economic evaluations.	How to develop a tool or guidelines that are feasible for data collection and analysis of cost data?
<b>Context-specific issues</b>					
Economic evaluations not included as a part of the decision-making process	No application of economic evaluation evidence and no strong political will and demand for higher quality evidences	Researchers, policy-makers in the context	Raising awareness and acceptability on economic evaluation among stakeholders especially policy-makers to increase political buy-in	1. Policy-makers may have limited knowledge and capacity to use economic evaluation evidences  2. Raising awareness on economic evaluation will expose policy-makers to this kind	1. What are factors that limit the use of economic evaluation in decision-making process in the context?  2. Will policy-makers apply economic evaluation evidence to decision-making process if they are well aware and understand this type of evidences?

Problems	Issues in the Use	Stakeholders / Affected Parties	Relevant Solution	Hypothesis	Example research Question(s)
				of study and improve their understandings on economic evaluations and their usefulness	
				3. There are context-specific barriers which result in economic evaluation not being perceived as useful or relevant to the context	3. What are the current opinions of stakeholders, especially policy-makers, towards economic evaluations and how can negative perceptions be overcome, if there are any?  4. Will other types of studies or approach, e.g. MCDA, be more accepted by stakeholders than the application of economic evaluation?
Limited local capacity to conduct or contextualize research	Limited or no supply for economic evaluation evidences	Policy-makers in the context	Incentivize as well as provide both formal and informal trainings for researchers to work on economic evaluation field.	1. Improvement in political demand for economic evaluation evidences will also results in limited availability of local research capacity	1. What are factors that will motivate researchers to work on economic evaluation?
				2. Economic evaluation research capacity can be built either through	2. How should training on economic evaluations be structured to ensure best

<b>Problems</b>	<b>Issues in the Use</b>	<b>Stakeholders / Affected Parties</b>	<b>Relevant Solution</b>	<b>Hypothesis</b>	<b>Example research Question(s)</b>
				formal, e.g. graduate trainings, and informal trainings, e.g. on the job trainings	capacity and performance of researchers produced?
Lack of funding for the necessary research	Unable to generate relevant research that can help inform decision-makings	Researchers	Raising awareness and acceptability on economic evaluation among stakeholders especially policy-makers to increase political buy-in	Government funding is limited and needs to be rationed among different necessary activities including health. Therefore enhancing health system efficiency may be excluded.	<p>1. What is policy-makers' willingness-to-pay for enhancing health system efficiency?</p> <p>2. What are the opportunity costs of not investing in economic evaluation research?</p>

### Appendix 3

Number	Full Name	Affiliation / Designation
1.	Jeonghoon Ahn	National Evidence-based Healthcare Collaborating Agency
2.	Jasmine Pwu	National Taiwan University
3.	Karen Hoffman	Priority Cost Effective Lessons for Systems Strengthening (PRICELESS SA)
4.	Melanie Bertram	World Health Organization
5.	Marianela Castillo Riquelme	Ministry of Health, Chile
6.	Yot Teerawattananon	Health Intervention and Technology Assessment Program
7.	Alia Luz	Health Intervention and Technology Assessment Program
8.	Benjarin Santatiwongchai	Health Intervention and Technology Assessment Program
9.	Karlena Luz	Health Intervention and Technology Assessment Program
10.	Saudamini Dabak	Health Intervention and Technology Assessment Program
11.	Dewi Indriani	World Health Organization
12.	Priska Apsari Primastuti	World Health Organization
13.	Raymond Hutubessy	World Health Organization
14.	Ryan Li	NICE International

## Appendix 4

The following details the questionnaire for the survey:

### Introduction

This survey is a part of a Health Intervention and Technology Assessment Program (HITAP) project funded by the International Decision Support Initiative (iDSI) to support the conduct of economic evaluations in low- and middle-income countries (LMICs). The results will be used to determine those research gaps and issues that prevent the conduct and the use of economic evaluation evidence in policy decision-making. They will also help the prioritization of research topics for the better conduct of economic evaluations in LMICs.

Are you a current or former researcher or research assistant with experience conducting (individually or as part of a team) an economic evaluation in a low- and middle-income country (LMIC)?

- Yes
- No
- I have filled out this survey before

To ensure that we gather the best responses, this survey is anonymous and your responses will in no way be connected to you or your affiliations. As such, please indicate your consent to the use of your responses for the Research Methods Agenda analysis and future presentations, publications, and materials.

- Yes
- No

### Background

This questionnaire will take no more than 15 minutes to answer. To begin, we would like to know more about you!

What is the highest level of education you have completed?

- Bachelors
- Post-graduate: Masters
- Post-graduate: Doctorate

Was economic evaluation a major part of your studies?

- Yes
- No

How many years have you been in the field of economic evaluation? Please write single numbers, e.g. 7. \_\_\_\_\_

What is your affiliation?

- Academic

- Public Health Institute
- Pharmaceutical Company
- Other, please specify: \_\_\_\_\_

In which country do you currently reside? (Dropdown)\_\_\_\_\_

In which areas do you work? Please note that this geographical grouping is based on the WHO regions.

- Southeast Asia** (Bangladesh, Bhutan, Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste)
- Africa** (Algeria, Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Cabo Verde, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Congo, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, South Africa, South Sudan, Swaziland, Togo, Uganda, Tanzania, Zambia, Zimbabwe)
- Americas** (Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, USA, Uruguay, Venezuela)
- Europe** (Albania, Andorra, Armenia, Austria, Azerbaijan, Belarus, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Luxembourg, Malta, Monaco, Montenegro, Netherlands, Norway, Poland, Portugal, Republic of Moldova, Romania, Russian Federation, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tajikistan, Macedonia, Turkey, Turkmenistan, Ukraine, United Kingdom, Uzbekistan)
- East Mediterranean** (Afghanistan, Bahrain, Djibouti, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, Yemen)
- West Pacific** (Australia, Brunei Darussalam, Cambodia, China, Cook Islands, Fiji, Japan, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, New Zealand, Niue, Palau, Papua New Guinea, Philippines, Korea, Samoa, Singapore, Solomon Islands, Tonga, Tuvalu, Vanuatu, Vietnam, Taiwan, Hong Kong)

Would you like to be informed of these results?

- Yes

No

If you answered yes to the question 9, please provide your email address and we will send you the results of this study. Thank you.

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Thank you for giving us your information.

The lists we outline in the next two pages are taken from HITAP's review of economic evaluation studies conducted in LMICs of a randomly selected sample of papers taken from the University of York's Center for Review and Dissemination and triangulated with a review of literature and expert opinion.

## Part 1: Technical Issues

Please answer the following questions regarding the methodology for economic evaluations.

The following are commonly met technical weaknesses that can hamper the quality and the use of economic evaluations in LMICs.

	<b>Issues</b>
A	Poor Reporting, e.g. <ul style="list-style-type: none"><li>• Perspective of analysis not stated</li><li>• Lack of details of the target population or sub-populations relating to the interventions being evaluated</li><li>• Lack of detail on the methods used to derive the measure of benefit</li><li>• Lack of details to enable checking of data sources for benefits / effectiveness</li><li>• Lack of details to enable checking of data sources for costs</li><li>• No details of the price year used as the basis of the cost analysis</li><li>• Methodology not presented in a clear and reproducible manner</li></ul>
B	A lack of commonly accepted standards for economic evaluation that's relevant to the LMIC for which the analysis is undertaken
	<b>Benefits / Effectiveness</b>
C	Lack of high quality local clinical data, where such data are critical to the decision
D	Clinical data not based on systematic review; or primary clinical data not compared with similar studies done elsewhere
E	Absence of locally-relevant health state preference data suitable for estimating QALYs or DALYs
	<b>Costs</b>
F	Insufficient data to conduct study from chosen perspective
G	Uncritical use of charges for cost data
	<b>Analysis</b>
H	Inappropriate choice of comparator (s)
I	Time horizon too short to capture relevant costs and health effects
J	All impacts implied by the chosen perspective not investigated
K	Unexplained differences in discount rates; or the discount rate used does not reflect reality in the local context
L	No incremental analysis
M	No, or inappropriate, sensitivity analysis
N	No budget constraints or thresholds considered
O	Equity and/or gender implications not considered
P	Generalizability not discussed

If there are any additional technical issues that present a challenge to the quality and use of economic evaluation in LMICs, please add the one that you consider the most relevant to the box below.

Q \_\_\_\_\_

From the list above (A-P or Q, including any issues you suggest), please choose 3 issues that you consider most important and rank them accordingly. Write the letter (A-R) corresponding to the issue you would like to highlight in the space provided below.

Most Important (1) \_\_\_\_\_

Second Most Important (2) \_\_\_\_\_

Third Most Important (3) \_\_\_\_\_

Please suggest potential solutions, tools, guidelines, materials, or other ways forward. You may suggest solutions specific to each of the issues you ranked or general solutions.

---

## **Part 2: Context-Specific Issues**

What other non-technical contextual factors affect the effective application and use of economic evaluation in LMICs?

	<b>Issues</b>
A	Economic evaluations not included as a part of the decision-making process
B	Lack of funding for the necessary research
C	Limited local capacity to conduct or contextualize research
D	Absence of local journal with a high quality reviewing processes
E	Misunderstandings and communications weaknesses between researchers, academia and end users of the evidence

If there are any additional context-specific issues that present a challenge to the use of economic evaluation in LMICs, please add the one that you consider the most relevant to the box below.

F \_\_\_\_\_

From the list above (A-E or F, including any issues you suggest), please choose the most important issue and write the letter (A-F) in the space below.

Most Important (1) \_\_\_\_\_

## **Part 3: Additional Information**

Broadly speaking, which of the two types of issues, technical and context-specific, do you consider to be the bigger impediment to better quality economic evaluation in LMICs?

- Technical Issues
- Context-specific Issue

To our knowledge, there is another ongoing project with a similar aim to that of this survey but placed in another context. The project is “Research Agenda for Health Economic Evaluation (RAHEE),” with the focus in Europe. If you have ever come across other projects with similar objectives to this study, please let us know below.

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Do you have any suggestion for the improvement of the questionnaire? Please specify which part of the survey was difficult to understand, unclear, or needs revision, and in what way(s).

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Thank you for taking our survey!

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