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SYSTEMATIC REVIEW

A Systematic Review of Health Economic Evaluations and Budget Impact Analyses to Inform Healthcare Decision-Making in Central America

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Abstract

Background Little is known about the quality, quantity and disease areas analysed by health economic research that inform healthcare decision-making in Central America. This study aimed to review the existing health economic evaluations (HEEs) and budget impact analyses (BIAs) evidence in Central America based on scope and reporting quality.

Methods HEEs and BIAs published from 2000 to April 2021 were searched in five electronic databases: PubMed, Embase, LILACS (Latin American and Caribbean Health Science Literature), EconLIT and OVID Global Health. Two reviewers assessed titles, abstracts and full texts of studies for eligibility. The quality appraisal for the reporting was based on La Torre and colleagues' version of the Drummond checklist and the ISPOR good practices for BIA. For each country, we correlated the number of studies by disease area with their respective burden of disease to identify under-researched health areas.

Results 102 publications were eligible for this review. Ninety-four publications reported a HEE, six publications reported a BIA, and two studies reported both a HEE and a BIA. Costa Rica had the highest number of publications ($n = 28$, 27.5%), followed by Guatemala ($n = 25$, 24.5%). Cancer and respiratory infections were the most common types of disease studied. Diabetes mellitus, chronic kidney diseases, and mental disorders were under-researched relative to their disease burden in most of the countries. The overall mean quality reporting score for HEE and BIA studies were 71/119 points (60%) and 7/10 points (70%), respectively; however, these assessments were made on different scales.

Conclusion In Central America, health economic research is sparse and is considered as suboptimal quality for reporting. The findings reported information useful to other low- and middle-income countries with similar advances in the application of economics to promote health policy decision-making.

1 Introduction

The road to achieving Universal Health Coverage (UHC) and ensuring equitable access to healthcare for everyone is a challenging ambition for the Latin American and the Caribbean countries (LAC), including those in Central America [1]. The Ministries of Health (MoHs) must deal with resource scarcity while making strides towards UHC and the enjoyment of the highest attainable standard of health, as the 1948 World Health Organization Constitution stated [2]. Considering that major challenge, the need and application of health technology assessment (HTA) and health economics analysis is crucial for health authorities and their decision-making process, particularly pertaining to the questions of whom to cover, which services to cover, and the proportion of costs to cover [3].

The Central American region is undergoing a demographic transition, with a low growth population rate and an increase in life expectancy at birth [4, 5]. Simultaneously, the region is experiencing an epidemiological transition whereby the transmissible disease mortality rate is decreasing while the noncommunicable disease mortality and morbidity rate is on the rise [6]. In 2019, health expenditure as a share of the Gross Domestic Product (GDP) in the region ranged from 6% in Belize to 8.4% in Nicaragua

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Key Points for Decision Makers

The production of health economic evaluations and budget impact analysis in Central America highlight that health economics, as a field of research informing health policy making, is at a promising stage of development.

We identified a low volume of health economics research for some health conditions (i.e., diabetes mellitus, chronic kidney diseases, and mental disorders) when compared to their burden of disease in the region.

The quality of reporting for the identified health economic evaluations informing decision-making was assessed as suboptimal, while for budget impact analysis was considered acceptable.

Future health economics studies in Central America need to consider the local population's health needs and adhere to the reporting guidelines to improve their usefulness in health decision-making.

[7]. Except for Costa Rica, there exist similarities across the health systems in Central America. For instance, the health systems in Central America are characterised by having low levels of insurance coverage, health expenditures primarily financed by the rich and a heavy concentration of the uninsured among the economically worse-off and rural populations [8–14]. This latter characteristic is likely exacerbated by the poor quality and low levels of physical access of public services to the poor. Lastly, the health systems have a relatively low ability to subsidise the poor, leaving them very vulnerable to catastrophic financial implications of ill health and impoverishment [8–14]. On the other hand, the health system of Costa Rica is characterised by having institutional stability, a high rate of healthcare coverage (94.7%), an integrated but well-differentiated provider arm, strong primary care, a degree of inter-sectoral coordination, and effective dialogue between users and health service providers [15, 16]. However, the increase in spending is not associated with an improvement in services, and the waiting queues are long and growing [15, 16].

There have been significant advances in Central America toward the application of HTA. For example, except for Belize and Nicaragua, all the countries from Central America are member states of the Pan American Health Organization (PAHO) HTA Network of the Americas (RedETSA) [17], which comprises representatives from the ministries of health, regulatory agencies, HTA agencies, PAHO/WHO collaborating centres, and non-profit educational and research institutions dedicated to promoting HTA to inform decision-making. In Central America, most HTA institutions belong to departments within the Ministry of Health and address the main goal of conducting assessments of efficacy, safety and efficiency aspects of health technologies to inform policy decision-making. However, these HTA institutions face several challenges. Two main challenges are to consolidate the link between HTA and decision making and increase the formal role of the HTA in the current healthcare decision making process [18]. Another challenge is increasing the resources (mainly budget and dedicated staff) to develop and sustain the technical capacity to produce HTA reports as well as health economic analysis and expand the scope of HTA to other non-pharmaceutical technologies [19].

Health economic evaluation (HEE) and budget impact analysis (BIA) are two common health economic analyses used to analyse the efficiency and affordability of alternative health interventions. Systematic reviews of HEE and BIA can inform the development of economic models, identify relevant studies for a particular decision-making process, identify the implicated cost-effectiveness or affordability trade-offs of health technologies [20], and may highlight methodological gaps to be strengthened in future studies. For HEE studies, a statistical analysis of publications, known as bibliometric analysis, showed a substantial body of HEE publications, especially in high-income countries [21]. Country-specific reviews of HEE studies were also performed in regions including LAC, Asia and Africa [22–32]. These studies concluded that there is an increasing bulk of HEE evidence, but most of them are of poor or fair quality. On the other hand, reviews of BIA have also been performed, most of which focused on drugs and medicines [33–37]. The reviews called attention to improving the quality of reporting and analysis for these studies. Unfortunately, all these reviews omitted a body of health economics research pertaining to the Central American region.

The current pattern of the rising cost of healthcare innovation, together with the demographic transition and an epidemiological shift from acute to chronic diseases, puts pressure on healthcare systems and budgets in the Central American region. In this context, reliable health economic research may become critical in shaping healthcare policy and priority settings. However, little is known about the quality, quantity and disease areas analysed by health economic research informing healthcare decision-making in Central America. To address this research gap, we provide an overview of the state of art and reporting quality of HEE and BIA published for Central American countries. Further, we aim to compare the distribution of the number of studies by disease area relative to its respective burden of disease in each country. Our findings may provide an empirical grounding for debate on the current state, future direction and priority setting for health economics research in the

Central American region and other low-and middle-income countries with similar advances in the application of economics to promote health policy decision-making.

2 Methods

The protocol of this review was registered on the International Centre for Reviews and Dissemination (CRD) Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42021265744. After a round of unanimous agreement, we included two additional outcomes (the cost-savings and the net monetary benefit) in the review in order to capture all the relevant economic studies performed in Central America. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines for reporting systematic reviews [38]. The 27-item PRISMA 2020 checklist is shown in the Electronic Supplementary Material 1 (ESM 1).

2.1 Search Strategy and Data Sources

A comprehensive search strategy was developed to identify published HEE and BIA studies pertaining to any Central American country: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama. We searched studies published from 1 January 2000 to 28 April 2021 in the following international and regional databases: PubMed, Embase, LILACS (Latin American and Caribbean Health Science Literature), EconLIT and OVID Global Health. Medical Subject Headings (MeSH) of PubMed were used to check the keywords applied in the search strings. The research team together with a librarian made careful checks to finalise the search strings and ensure that the search increased the specificity without compromising the sensitivity. The search strings are shown in ESM 2.

2.2 Type of Outcome Measures

We defined the primary outcome as the incremental cost-effectiveness ratio (ICER): cost per quality-adjusted-life-year (QALY), cost per disability-adjusted-life-year (DALY), cost per life-year saved and cost per illness averted. The absolute or relative budget impact was also considered as a primary outcome measure. Other outcomes include cost-savings and net monetary benefit, with the latter defined as a statistic that represents the value of an intervention in monetary terms when a willingness-to-pay threshold for a unit of benefit (e.g., a measure of health outcome or QALY) is known.

2.3 Inclusion and Exclusion Criteria

We included full HEEs, defined as those studies comparing both costs and outcomes of two or more health interventions, and full BIAs, defined as studies that measure the financial impact of implementing an intervention on the healthcare budget for a given number of patients in a specific population. For both HEEs and BIAs, we included full articles and abstracts that met the inclusion criteria, whether they were model-based studies or not. We excluded study protocols and cost of illness (COI) studies not comparing cost and outcomes of interventions. Editorials, letters to editors, opinion papers, and meeting reports were excluded.

2.4 Screening and Data Extraction

Two health economists (CRR and AP) selected the studies based on a two-stage screening process. First, the titles and abstracts of all the initial search results were reviewed. Based on the screening of titles and abstracts, in the second stage of the screening process, the potentially relevant studies were further examined based on the content of the full texts. The discrepancies during the study selection were solved by consensus of the research team. The screening process was devised using the COVIDENCE® software [39]. In the final stage of the study selection, we hand-searched the reference lists of each of the papers selected for inclusion, to ensure that we had not missed any key publications.

Two independent reviewers (CRR and AP) extracted all relevant information using a standardised data extraction form in Microsoft Office Excel. The data extraction form was pre-piloted and was developed to collect general and methodological data from the selected studies. To develop this form, we consulted the Cochrane Handbook for Systematic Review of Interventions [40], previous systematic reviews of health economic evaluations performed in other low- and middle-income countries (LMICs) [30, 31] and other quality criteria used in previous systematic reviews of BIA [33–37, 41].

2.5 Critical Appraisal and Quality Assessment for Reporting

The critical appraisal and quality assessment for reporting HEE studies was performed using the Drummond checklist developed by Drummond and colleagues [42]. To give a composite score to each study based on its quality of reporting, we used a weighted version of the Drummond checklist developed by La Torre and colleagues [43]. The composite score ranges from zero to 119 points. We reported the percentage of total points attained. For the journal articles only,

we compared the composite scores according to the country and other characteristics of interest by using a t-test.

The ISPOR Task Force on Good Research Practices [44] and the practical guide for BIAs of healthcare interventions [45] were used to perform the critical appraisal and reporting quality assessment for BIA studies, based on the level of adherence to these guidelines. The instrument assesses ten quality-of-reporting items, with the following possible answer: yes/no/does not apply. A positive answer counted as one point for each item, and a negative response counted as zero points. The total positive punctuation was the sum of all the positive answers that the study attained. We reported the percentage of total possible points.

All the critical appraisal and quality assessment instruments used in this review can be accessed in ESM 3.

2.6 Data Synthesis and Analysis

Detailed revisions were performed to classify studies by country studied, which then were mapped using Microsoft Office Excel. Studies covering a set of countries (defined here as multi-country studies) but including countries from the Central American region were individually reviewed and manually classified. In addition, for each study we individually reviewed the date of publication and later a time graph was plotted. The study interventions were classified by the authors according to the level of care in the following categories: primary, secondary or tertiary. Descriptive statistical analysis including absolute and relative frequencies were used to describe the characteristics of the studies.

We compared the distribution of the number of studies by disease area, relative to its respective burden of disease in each country. Comparisons are presented graphically with scatter plots comparing the volume of studies and burden of disease by proportion of total, disaggregated by country, which allowed us to both assess the correlation and to identify health-area outliers that merit deeper exploration. We classified the studies according to the type of disease, based on the classification of diseases of the Global Burden of Disease (GBD), developed by the Institute for Health Metrics and Evaluation at the University of Washington. This classification allowed comparability with the 2019 GBD estimates [46]. The burden of disease was measured using the DALYs attributable to each disease.

Based on the outcomes analysed [47, 48], we classified HEE studies into categories of cost-benefit, cost-effectiveness, cost-minimization or cost-utility. Further, based on the conclusion of the study we classified the interventions analysed in the HEE studies as cost-effective or not cost-effective. The classification of the interventions was described using absolute and relative frequencies, per country.

3 Results

A total of 4,469 studies were identified from the databases and two additional studies were identified through other sources (manual reference checking) as shown in Fig. 1. After removing duplicates (n = 73), the remaining 4,398 studies were screened by applying the inclusion criteria to the titles and abstracts. A total of 4237 studies were excluded in the first-stage screening and the remaining 161 studies were identified as eligible for full-text assessment. Two studies had originally appeared to meet the inclusion criteria, but in the end were excluded because one was a theoretical/discussion article (unsuitable study design) [49] and the other did not report any outcome of interest for the review [50]. Ultimately, 102 studies were eligible for this systematic review [51–152].

3.1 General Characteristics of Included Studies

Of the 102 included publications, 94 studies reported a HEE, six studies reported a BIA, and two studies reported both a HEE and a BIA. In total, we included 96 studies reporting HEEs and eight studies reporting BIAs. Figure 2 presents the individual countries most frequently studied. The sum of the studies does not add up to 102 since some studies included in the review analysed more than one individual country from Central America. Costa Rica was the setting in 28 studies (27.5%), followed by Guatemala (n = 25, 24.5%), Nicaragua (n = 22, 21.6%), Panama (n = 22, 21.6%), Honduras (n = 17, 16.6%), El Salvador (n = 15, 14.7%) and Belize (n = 4, 3.9%).

The time distribution of studies is presented in ESM 4. The most productive year was 2015 with 15 studies published, followed by 2013 (n = 13) and 2014 (n = 12).

ESM 5 reports the general characteristics of included studies. For the 96 HEE studies, 27% of them conducted a multi-country HEE. For the individual country population, 20% of the HEE studied population were from Costa Rica. Approximately half of all the HEEs were published as journal articles (52%), while the remaining HEEs were published as abstracts in conferences/congresses (48%). The oldest HEE included was published in 2005 [123]. Cancer (25%) and respiratory infections and tuberculosis (23%) were the most common types of disease studied in HEEs. On the other hand, Panama had three BIA studies, representing 38% of the total BIAs included in this review. Only three out of eight BIA were published as journal articles. The oldest BIA included was published in 2008 [148]. Half of all the BIAs studied cancer.

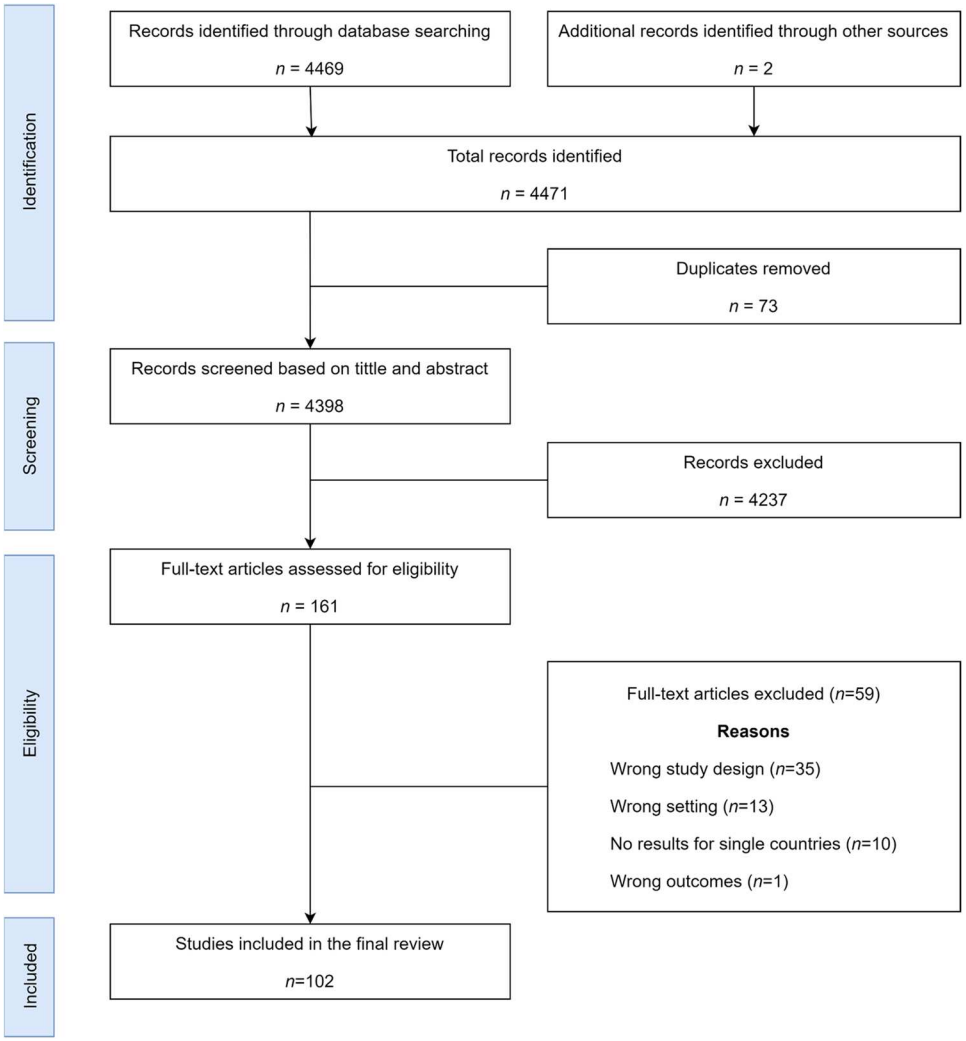

Fig. 1 Flow chart showing the literature search strategy. Source: adapted from Page and colleagues [38]

3.2 Scope and Methodological Characteristics of the Health Economic Evaluations (HEEs) in Central America

The 96 publications reporting HEEs were classified according to the type of HEE: cost-benefit, cost-effectiveness, cost-minimization or cost-utility. Considering this classification, cost-effectiveness was the most frequent (n = 56), followed by cost-utility (n = 30), cost-benefit (n = 9) and cost-minimization (n = 1), as shown in ESM 6.

Table 1 shows the scope and methodological characteristics of HEEs in Central America. For journal articles and abstracts, most of the HEEs in Central America used a public third-party-payer perspective of analysis (36% and 54.3%, respectively), followed by the societal perspective (24% and 15.2%, respectively). For those studies that adopted the societal perspective, most of them reported out-of-pocket expenditures (such as cost of transportation) and productivity loss costs. In general, the most common type of cost included was direct medical costs (46% of journal articles and 78.3% of abstracts). In most cases, the cost estimation approach was not clear or not stated (60% of journal articles and 67.4% of abstracts), and the bottom-up methodology was the most frequent cost estimation approach reported (14% of published articles and 19.6% of abstracts). For all types of publications, more than 30% of the HEEs used a lifetime time horizon. In 30% of the journal articles the time horizon of the study was not clear or not stated, while the percentage was 15.2% for the abstracts. QALYs and DALYs were the most frequent health outcomes measured in HEEs for both types of publications. Moreover, the most common discount rates applied were 3% (50% of all the journal articles) and 5% (12% of all journal articles) irrespective of the type of publication. The discount rate was not clear or not stated in 26% of the journal articles and in 15.2% of the abstracts.

For both types of publications, the most common threshold to define an intervention as cost-effective was 1 gross domestic product (GDP) and 3 GDP. However, in 42% of the journal articles and in 34.8% of the abstracts the threshold was not clear or not stated. We found that most of the studies

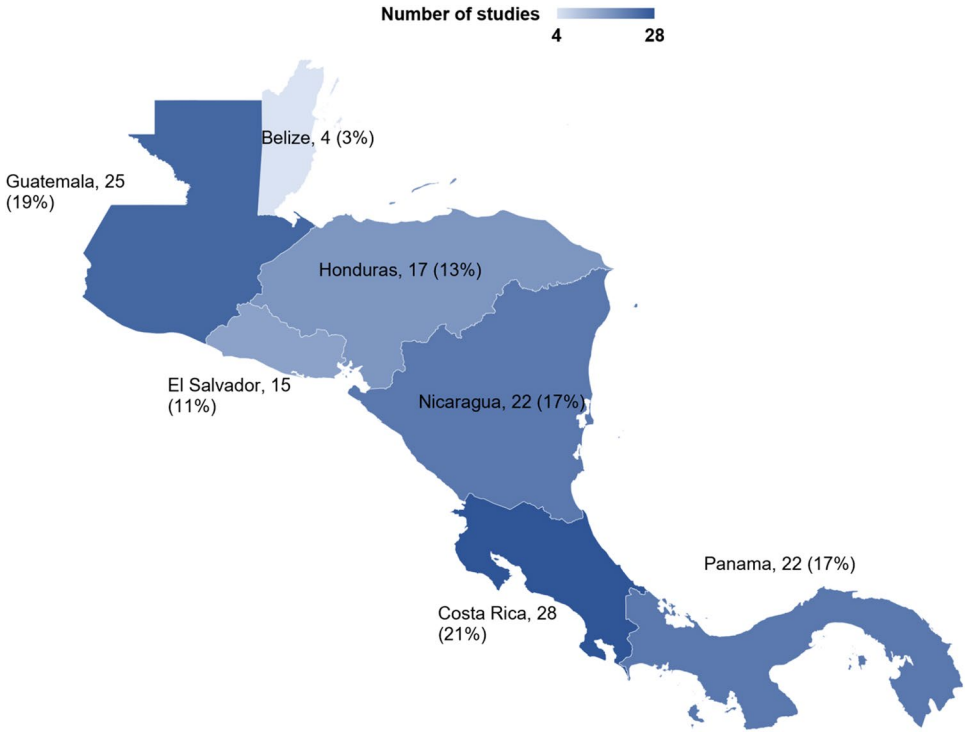

Fig. 2 Number of studies in each country in Central America. The intensity of shading reflects the number of studies from each country over the 21-year period from 1 January 2000 to 28 April 2021.The sum of the studies does not add up to 102 since some studies included in the review analysed more than one individual country from Central America.

(68.8%), whether published as abstracts or not, did not state the use of any reporting guideline for cost-effectiveness analysis. The funding agency was not clear or not stated in 50% of the published studies and in 63% of the abstracts. Authors reported conflicts of interest in 18% of the journal articles and in 19.6% of the abstracts, but in 58% and 63% of the journal articles and abstracts, respectively, the conflicts of interest were not clear or not stated. In most of the cases (66% for journal articles and 43.5% for abstracts), the primary author had his institution of affiliation in a foreign country. None of the primary authors had their institutional affiliation in Belize or Nicaragua.

For journal articles, the university was the type of affiliation most common for primary authors (50%), followed by pharmaceutical companies (16%). Most journal articles and abstracts involved international authors, and the mean number of authors per study was 5.1 (standard deviation: 2.6) for journal articles and 5.3 (standard deviation: 2.4) for abstracts. Modelling as a study design was most frequently used among journal articles (66%) and abstracts (91.3%). Most studies used US dollars as the currency (94% of journal articles and 87% of abstracts). For journal articles, deterministic sensitivity analysis only (36%), probabilistic sensitivity analysis only (16%), and both probabilistic and deterministic analysis (14%) were the most frequent types of sensitivity analysis performed. However, in 22% of journal articles, sensitivity analysis was not stated or not performed.

For journal articles, the most common types of intervention were pharmaceutical (28%), public health programme (26%), and vaccine (24%). In addition, the level of care most studied was primary care (64%), and the nature of care most studied was treatment (52%). Nearly half (48%) of the journal articles in Central America concluded that the studied intervention was cost-effective at the threshold defined, 24% concluded that the intervention was cost-saving, and 14% concluded that the intervention was probably cost-effective at the threshold defined. In 6% of the studies the conclusion was unclear, and in 4% of the studies the intervention was not cost-effective at the threshold defined. The distribution was similar for the studies published as abstracts.

The ESM 7 reports the classification of the HEE interventions according to the conclusion of the study. A dominant intervention was reported in 53% of the HEEs in Panama (the country that has the most prevalent studies with dominant interventions) and in 25% of HEEs in Honduras (the country that has the least frequent studies with dominant interventions). All four of the studies performed in Belize concluded that the intervention under analysis was cost-effective, while 75% of the studies reported the same in Honduras. For Costa Rica, El Salvador, Guatemala, Nicaragua and Panama, the percentage of studies with cost-effective interventions were 50%, 47%, 29%, 48% and 37%, respectively. In 8%, 5% and 4% of the HEEs performed in Costa Rica, Guatemala and Nicaragua, respectively, the intervention was reported as not cost-effective.

Table 1 Scope and methodological characteristics of the health economic evaluations in Central America

Characteristic	Journal articles ($n = 50$)		Abstracts ($n = 46$)		Overall ($n = 96$)	
	Frequency	%	Frequency	%	Frequency	%
Perspective of analysis						
Healthcare provider	8	16.0%	7	15.2%	15	15.6%
Private third-party payer	2	4.0%	1	2.2%	3	3.1%
Social security third-party payer	3	6.0%	2	4.3%	5	5.2%
Public third-party payer	18	36.0%	25	54.3%	43	44.8%
Societal	12	24.0%	7	15.2%	19	19.8%
Not clear	7	14.0%	4	8.7%	11	11.5%
Cost included						
Direct medical costs alone	23	46.0%	36	78.3%	59	61.5%
Direct and indirect medical costs	12	24.0%	6	13.0%	18	18.8%
Direct program and medical costs	12	24.0%	2	4.3%	14	14.6%
Not clear	3	6.0%	2	4.3%	5	5.2%
Cost estimation approach						
Bottom-up	7	14.0%	9	19.6%	16	16.7%
Top-bottom	1	2.0%	2	4.3%	3	3.1%
Bottom-up and top-bottom	2	4.0%	0	0.0%	2	2.1%
Indirect estimations	6	12.0%	3	6.5%	9	9.4%
Top-bottom and indirect estimation	4	8.0%	1	2.2%	5	5.2%
Not clear or not stated	30	60.0%	31	67.4%	61	63.5%
Time horizon						
1-5 years	8	16.0%	12	26.1%	20	20.8%
>5 years but not lifetime	10	20.0%	13	28.3%	23	24.0%
Lifetime	17	34.0%	14	30.4%	31	32.3%
Not clear or not stated	15	30.0%	7	15.2%	22	22.9%
Health outcome measure						
Clinical endpoints	4	8.0%	7	15.2%	11	11.5%
DALY	18	36.0%	9	19.6%	27	28.1%
Illness prevented	4	8.0%	4	8.7%	8	8.3%
Life expectancy	0	0.0%	3	6.5%	3	3.1%
Life years saved	3	6.0%	1	2.2%	4	4.2%
QALY	13	26.0%	19	41.3%	32	33.3%
Other	8	16.0%	3	6.5%	11	11.5%
Base-case discount rate						
0%	3	6.0%	9	19.6%	12	12.5%
3%	25	50.0%	17	37.0%	42	43.8%
3.5%	2	4.0%	1	2.2%	3	3.1%
5%	6	12.0%	10	21.7%	16	16.7%
Other rate	1	2.0%	2	4.3%	3	3.1%
Not clear or not stated	13	26.0%	7	15.2%	20	20.8%
Threshold used to define cost-effectiveness						
1 GDP per capita	14	28.0%	7	15.2%	21	21.9%
2 GDP per capita	1	2.0%	1	2.2%	2	2.1%
3 GDP per capita	14	28.0%	17	37.0%	31	32.3%
Multiple thresholds	0	0.0%	1	2.2%	1	1.0%
Other	0	0.0%	4	8.7%	4	4.2%
Not clear or not stated	21	42.0%	16	34.8%	37	38.5%
Guideline used for cost-effectiveness						
CHEERS	1	2.0%	1	2.2%	2	2.1%

Table 1 (continued)

Characteristic	Journal articles ($n = 50$)		Abstracts ($n = 46$)		Overall ($n = 96$)	
	Frequency	%	Frequency	%	Frequency	%
WHO-CHOICE	9	18.0%	7	15.2%	16	16.7%
Multiple guidelines	5	10.0%	4	8.7%	9	9.4%
Other	1	2.0%	2	4.3%	3	3.1%
Not stated	34	68.0%	32	69.6%	66	68.8%
Funding agency						
Non-governmental organisation	5	10.0%	3	6.5%	8	8.3%
Pharmaceutical company	3	6.0%	3	6.5%	6	6.3%
Research Institute/University	1	2.0%	0	0.0%	1	1.0%
United Nations or multilateral aid agency	7	14.0%	1	2.2%	8	8.3%
University	3	6.0%	1	2.2%	4	4.2%
None as stated by authors	2	4.0%	0	0.0%	2	2.1%
Multiple funding agencies	4	8.0%	7	15.2%	11	11.5%
Other	0	0.0%	2	4.3%	2	2.1%
Not clear or not stated	25	50.0%	29	63.0%	54	56.3%
Authors report conflict of interest?						
Yes	9	18.0%	9	19.6%	18	18.8%
No conflict of interests to declare	12	24.0%	8	17.4%	20	20.8%
Not clear or not stated	29	58.0%	29	63.0%	58	60.4%
Country affiliation of lead author						
Belize	0	0.0%	0	0.0%	0	0.0%
Costa Rica	10	20.0%	18	39.1%	28	29.2%
El Salvador	3	6.0%	0	0.0%	3	3.1%
Guatemala	0	0.0%	1	2.2%	1	1.0%
Honduras	0	0.0%	1	2.2%	1	1.0%
Nicaragua	0	0.0%	0	0.0%	0	0.0%
Panama	4	8.0%	6	13.0%	10	10.4%
Foreign country	33	66.0%	20	43.5%	53	55.2%
Lead author's type of affiliation						
Government	5	10.0%	3	6.5%	8	8.3%
Hospital	8	16.0%	2	4.3%	10	10.4%
Pharmaceutical company	8	16.0%	23	50.0%	31	32.3%
Research Institute	1	2.0%	3	6.5%	4	4.2%
University	25	50.0%	13	28.3%	38	39.6%
Other	3	6.0%	2	4.3%	5	5.2%
Involvement of international authors						
No	5	10.0%	5	10.9%	10	10.4%
Yes	45	90.0%	41	89.1%	86	89.6%
Average number of authors						
Mean (standard deviation)	5.14	2.64	5.33	2.36	5.23	2.50
Study design						
Before-after study	1	2.0%	0	0.0%	1	1.0%
Cohort study	2	4.0%	0	0.0%	2	2.1%
Hospital administrative or program data	12	24.0%	4	8.7%	16	16.7%
Trial based	2	4.0%	0	0.0%	2	2.1%
Modelling	33	66.0%	42	91.3%	75	78.1%
Type of model						
Decision tree	15	30.0%	16	34.8%	31	32.3%
Dynamic transmission model	4	8.0%	2	4.3%	6	6.3%

Table 1 (continued)

Characteristic	Journal articles ($n = 50$)		Abstracts ($n = 46$)		Overall ($n = 96$)	
	Frequency	%	Frequency	%	Frequency	%
Markov model	14	28.0%	21	45.7%	35	36.5%
Patient-level simulation	2	4.0%	0	0.0%	2	2.1%
Other	0	0.0%	1	2.2%	1	1.0%
Not clear	3	6.0%	4	8.7%	7	7.3%
Does not apply	12	24.0%	2	4.3%	14	14.6%
Currency						
Local currency	2	4.0%	4	8.7%	6	6.3%
US dollars	47	94.0%	40	87.0%	87	90.6%
International dollars	1	2.0%	1	2.2%	2	2.1%
Both local currency and US dollars	0	0.0%	1	2.2%	1	1.0%
Type of sensitivity analysis performed						
Deterministic alone	18	36.0%	16	34.8%	34	35.4%
Probabilistic alone	8	16.0%	16	34.8%	24	25.0%
Probabilistic and deterministic	7	14.0%	9	19.6%	16	16.7%
None or not stated	11	22.0%	3	6.5%	14	14.6%
Not clear	6	12.0%	2	4.3%	8	8.3%
Type of intervention						
Pharmaceutical	14	28.0%	24	52.2%	38	39.6%
Public health programme	13	26.0%	6	13.0%	19	19.8%
Screening	4	8.0%	5	10.9%	9	9.4%
Service delivery	6	12.0%	3	6.5%	9	9.4%
Vaccine	12	24.0%	7	15.2%	19	19.8%
Other	1	2.0%	1	2.2%	2	2.1%
Level of care provision						
Primary	32	64.0%	27	58.7%	59	61.5%
Secondary	11	22.0%	12	26.1%	23	24.0%
Tertiary	7	14.0%	7	15.2%	14	14.6%
Nature of care						
Preventive	23	46.0%	19	41.3%	42	43.8%
Treatment	26	52.0%	26	56.5%	52	54.2%
Palliative	1	2.0%	1	2.2%	2	2.1%
Conclusion on the health technology under study						
Cost-saving	12	24.0%	8	17.4%	20	20.8%
Cost-effective at the threshold defined	24	48.0%	27	58.7%	51	53.1%
Probably cost-effective at the threshold defined	7	14.0%	4	8.7%	11	11.5%
Cost-effective but no threshold defined	2	4.0%	2	4.3%	4	4.2%
Not cost-effective at the threshold defined	2	4.0%	1	2.2%	3	3.1%
Not clear	3	6.0%	4	8.7%	7	7.3%
Considering the budget impact?						
No	49	98.0%	45	97.8%	94	97.9%
Yes	1	2.0%	1	2.2%	2	2.1%

CHEERS the Consolidated Health Economic Evaluation Reporting Standards statement, *DALYs* disability-adjusted life-years, *GDP* gross domestic product, *QALYs* quality-adjusted life-years, *WHO-CHOICE* the World Health Organisation Guide to Cost-Effectiveness Analysis

3.3 Scope and Methodological Characteristics of Budge Impact Analyses (BIAs) in Central America

The scope and methodological characteristics of the identified BIAs in Central America are shown in Table 2. Two out of three BIAs published as journal articles used the healthcare-provider perspective of analysis, and three out of eight studies published as abstracts used the public third-party-payer perspective. Among journal articles, one study used 1-year as a time horizon, another study used a 5-year time horizon, and the other one used a 7-year time horizon. No studies reported the use of a guideline for BIAs.

In all the studies published as abstracts the funding agency was not clear, while all the studies published as journal articles stated the funding agency. In one BIA published as a journal article the authors reported conflicts of interest. In all BIAs published as abstracts the conflicts of interest were not clear or not reported. Two out of three journal articles have the leading author affiliated to a foreign country, while three abstracts (40%) have an author affiliated to an institution based in Costa Rica. Irrespective of the type of publication, the involvement of international authors is common. Two out of three studies published as journal articles used US dollars as the currency while all abstracts used US dollars as the currency. One-third of the journal articles used modelling as the design of the study. All the journal articles used deterministic sensitivity analysis, while 80% of the abstracts did not apply deterministic sensitivity analysis or were not stated. Two journal articles analysed a public health programme while one analysed a service delivery. All the abstracts analysed a pharmaceutical intervention. For the journal articles, primary level of care was analysed in two studies, and one study analysed the tertiary level of care. The preventive nature of care was analysed in two journal articles (67%). All the studies published as journal articles reported a positive budget impact, while 40% of the studies published as abstracts reported a cost-saving budget impact.

3.4 Quality of Reporting of HEE Studies in Central America

An assessment of the quality of reporting of HEE studies in Central America is presented in ESM 8. The quality assessment of reporting is presented according to the type of publication (journal article or abstract). HEE studies in Central America were generally of good-quality reporting in terms of stating the research question (100%), describing the alternatives being compared (100%), comparing relevant alternatives (99%), stating the form of economic evaluation (89%), answering the study question (100%), and forming the conclusion from the data reported (99%). However, HEE studies had major limitations for reporting, especially those published as abstracts. Abstracts missed in stating the economic importance of the research question (20%), stating and justifying the perspective(s) of the analysis (30%), stating the rationale for choosing both the comparators and interventions analysed (26%), providing details about the effectiveness inputs used (4%), stating the methods to valuing health states or other benefits (9%), and describing the methods for the estimation of quantities of healthcare resources and its unit costs (2%) and justifying the choice of variable for the sensitivity analysis (2%). None of the abstracts gave details of the currency, price adjustments for inflation, or currency conversion, or presented in a disaggregated as well as in an aggregated form the major outcomes. On the other hand, most of the journal articles failed to report separately the quantity of health resources from their unit costs (60%) and failed to present the major outcomes in a disaggregated form as well as in an aggregate form (60%). Only half of all the studies gave details about the statistical tests used or confidence intervals for stochastic data.

The overall quality of reporting score of HEE studies in Central America is reported in the ESM 9. The overall quality of reporting score was 60% (71 points out of 119 points). For the abstracts, the overall mean quality of reporting score was 37% (44 points out of 119 points), while for the journal articles the overall mean quality of reporting score was 81% (96 points out of 119 points). Among the journal articles, the quality of studies was significantly higher in El Salvador ($p = 0.0431$), those with involvement of an international author ($p < 0.001$), those with a preventive nature of care ($p = 0.0468$), or those that used a lifetime time horizon ($p = 0.0161$).

3.5 Quality of Reporting of BIA Studies in Central America

ESM 10 provides a summary of the quality of reporting of BIA in Central America, according to the adherence to the ISPOR Task Force on Good Research Practices [44] and to the practical guide for BIA of healthcare interventions [45]. The overall mean quality of reporting of the BIA in Central America was acceptable, fulfilling on average 70% of the quality of reporting items (7 out of 10 points). For journal articles, the quality of reporting was 92%, while for the abstracts it was 55%. Fiedler [148] and Campos [106] are the two studies with the highest quality of reporting (100%), while Peralta-Acon (50%) [147] and Castro (44%) [64] are the two studies with the lowest quality of reporting. Overall, most of the studies (75%) failed to provide the model framework, failed to describe the cost analysis approach, or failed to provide the source of the market shares (where applicable).

Table 2 Scope and methodological characteristics of the budget impact analyses in Central America.

Characteristic	Journal articles ($n = 3$)		Abstracts ($n = 5$)		Overall ($n = 8$)	
	Frequency	%	Frequency	%	Frequency	%
Perspective of analysis						
Healthcare provider	2	66.67%	1	20.00%	3	37.5
Public third-party payer	1	33.33%	2	40.00%	3	37.5
Social security third-party payer	0	0.00%	2	40.00%	2	25.0
Budget impact horizon, in years						
1	1	33.33%	0	0.00%	1	12.5
3	0	0.00%	2	40.00%	2	25.0
5	1	33.33%	2	40.00%	3	37.5
7	1	33.33%	0	0.00%	1	12.5
Not clear	0	0.00%	1	20.00%	1	12.5
Cost estimation approach						
Bottom-up	1	33.33%	0	0.00%	1	12.5
Top-bottom	1	33.33%	0	0.00%	1	12.5
Indirect estimation	0	0.00%	1	20.00%	1	12.5
Not clear	1	33.33%	4	80.00%	5	62.5
Guideline for budget impact analysis						
Not clear or not stated	3	100.00%	5	100.00%	8	100.0
Funding agency						
Non-governmental organisation	1	33.33%	0	0.00%	1	12.5%
Multiple funding agencies	1	33.33%	0	0.00%	1	12.5%
State/national government	1	33.33%	0	0.00%	1	12.5%
Not clear	0	0.00%	5	100.00%	5	62.5%
Authors report conflict of interests?						
Yes	1	33.33%	0	0.00%	1	12.5
No conflict of interests to declare	1	33.33%	0	0.00%	1	12.5
Not clear or not stated	1	33.33%	5	100.00%	6	75.0
Country affiliation of lead author						
Belize	0	0.00%	0	0.00%	0	0
Costa Rica	0	0.00%	3	60.00%	3	37.5
El Salvador	0	0.00%	0	0.00%	0	0
Guatemala	0	0.00%	0	0.00%	0	0
Honduras	0	0.00%	0	0.00%	0	0
Nicaragua	0	0.00%	0	0.00%	0	0
Panama	1	33.33%	0	0.00%	1	12.5
Foreign country	2	66.67%	2	40.00%	4	50.0
Lead author's type of affiliation						
Government	1	33.33%	1	20.00%	2	25.0
Pharmaceutical company	0	0.00%	2	40.00%	2	25.0
University	1	33.33%	0	0.00%	1	12.5
Other	1	33.33%	2	40.00%	3	37.5
Involvement of international authors						
Yes	2	66.67%	3	60.00%	5	62.5
No	1	33.33%	2	40.00%	3	37.5
Average number of authors						
Mean (standard deviation)	5.33	2.08	3.40	1.14	4.13	1.73
Currency						
US dollars	2	66.67%	5	100.00%	7	87.5
Both local currency and US dollars	1	33.33%	0	0.00%	1	12.5

Table 2 (continued)

Characteristic	Journal articles ($n = 3$)		Abstracts ($n = 5$)		Overall ($n = 8$)	
	Frequency	%	Frequency	%	Frequency	%
Study design						
Hospital administrative data or program data	2	66.67%	1	20.00%	3	37.5
Modelling	1	33.33%	4	80.00%	5	62.5
Type of sensitivity analysis performed						
Deterministic	3	100.00%	1	20.00%	4	44.4
None or not stated	0	0.00%	4	80.00%	5	55.6
Type of intervention						
Pharmaceutical	0	0.00%	5	100.00%	5	62.5
Public health programme	2	66.67%	0	0.00%	2	25.0
Service delivery	1	33.33%	0	0.00%	1	12.5
Vaccine	0	0.00%	0	0.00%	0	0
Level of care provision						
Primary	2	66.67%	0	0.00%	2	25.0
Secondary	0	0.00%	3	60.00%	3	37.5
Tertiary	1	33.33%	2	40.00%	3	37.5
Nature of care						
Preventive	2	66.67%	0	0.00%	2	25.0
Treatment	1	33.33%	5	100.00%	6	75.0
Conclusion of the study						
Positive budget impact	3	100.00%	3	60.00%	6	75.0
Cost-saving	0	0.00%	2	40.00%	2	25.0

3.6 Correlation Between the Number of Studies by Disease Area Relative to its Burden of Disease

Figure 3 depicts the degree of the correlation between the number of studies by disease area, relative to its respective burden of disease in each country. Interventions to address cancer absorbed a great proportion of the total number of studies per country and seem to be over-researched relative to the disease burden. HIV/AIDS appears to be well studied relative to its disease burden in some countries, although no studies were found for Belize or Costa Rica. Moreover, respiratory infections and tuberculosis seem to be well studied in all countries, except Belize and Panama, where no studies were found. By contrast, interventions to address skin and subcutaneous diseases, diabetes mellitus, chronic kidney diseases, mental disorders or injuries appear to be substantially under-researched or not yet well researched relative to their disease burden in most of the countries.

4 Discussion

This study aimed to review and critically appraise the scope and reporting quality of health economics research in Central America. Our review yielded a total of 96 HEEs and eight BIAs published from 2000 to 2021. Over a quarter of all the studies were multi-country studies (26%). Moreover, over half of all HEEs and three out of eight BIAs were published as journal articles. The average quality reporting score for HEE was 81% for journal articles and 37% for abstracts. For the BIA included, the average quality of reporting score was 70%, ranging from 55% for abstracts to 92% for published articles.

4.1 Characteristics of the Studies

We found that the majority of the HEEs are cost-effectiveness analysis (60%), as reported in earlier systematic reviews of HEE studies in other LMIC settings [23, 29, 32]. Based on this review, Costa Rica had the highest absolute number of studies published compared to the rest of Central American countries. On the other hand, the bottom-up approach, which is the most transparent and precise method of cost estimation [153], was applied only in 16% of HEEs and in 12.5% of BIAs. This raises concerns about the accuracy and methodological quality of the cost estimations performed in the identified studies. In addition, a large proportion of studies did not clearly report conflicts of interest (60% for HEE studies and 75% for BIA studies) or sources of funding for the study (56% for HEEs and 62.5% for BIAs). These findings are quite

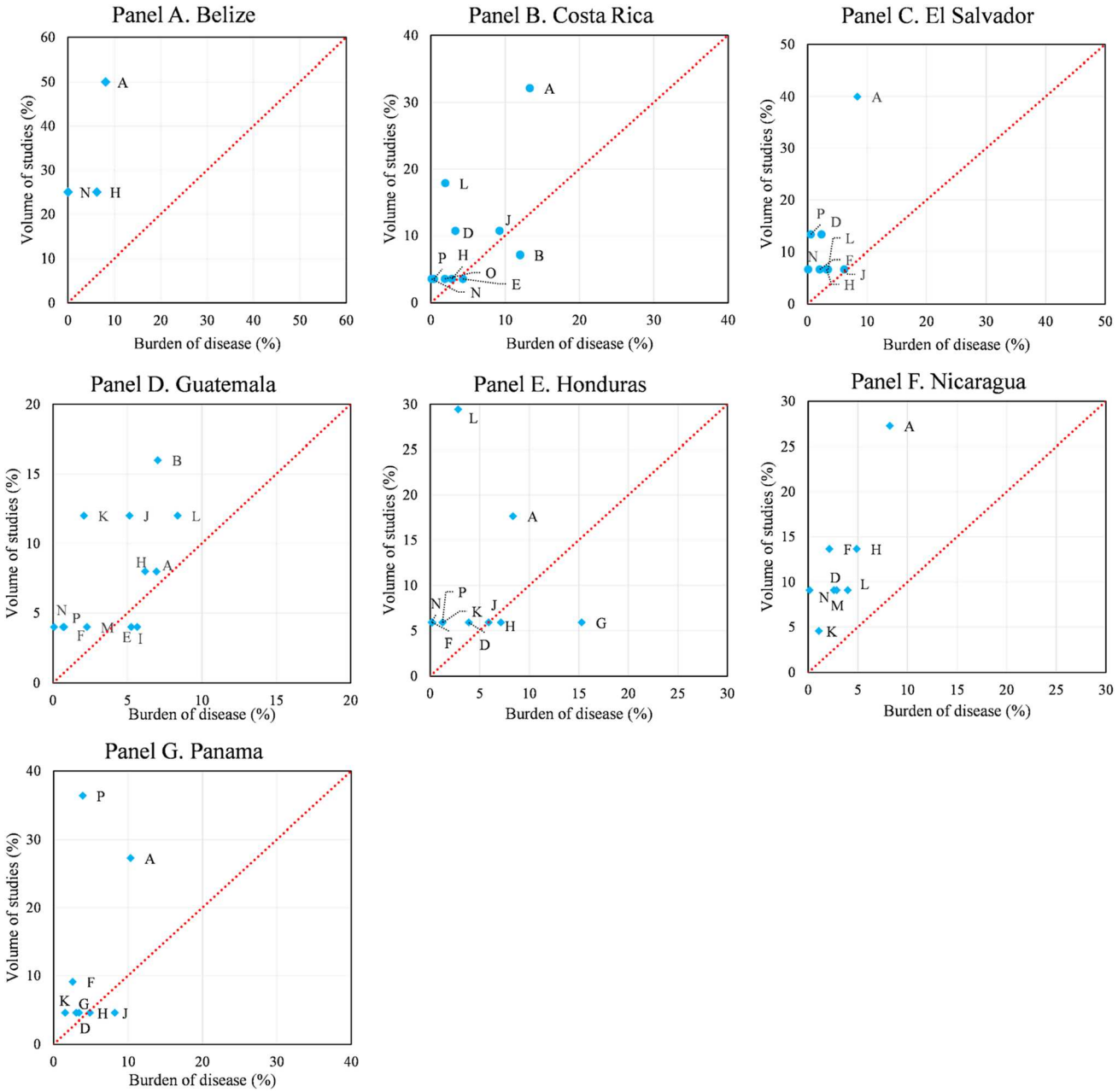

Fig. 3 Correlation between the types of diseases studied and the burden of disease in Central America. *A* cancer, *B* cardiovascular diseases, *C* chronic kidney diseases, *D* chronic respiratory diseases, *E* diabetes mellitus, *F* HIV/AIDS, *G* injuries, *H* maternal and neonatal disorders, *I* mental disorders, *J* musculoskeletal disorders, *K* nutritional deficiencies, *L* respiratory infections and tuberculosis, *M* sense organ diseases, *N* sexually transmitted infections excluding HIV/AIDS, *O* skin and subcutaneous diseases, *P* other infectious diseases.

similar to those reported in other LMIC contexts such as Zimbabwe (62%) [24], Nigeria (55%) [25] and South Africa (45%) [27].

The most common thresholds to determine the cost-effectiveness of an intervention in HEE studies were 1 and 3 GDP per capita, following the report of the WHO Commission on Macroeconomics and Health [154]. However, in spite of the widespread use of these thresholds, there remains limited understanding on what those thresholds represent and how they can be derived, and they have been extensively criticised for lacking scientific rationale to justify their use in resource allocation decisions [155–158]. For example, Marseille and colleagues argue that relying on these thresholds would omit any consideration of what is truly efficient and affordable and reduces the value of cost-effectiveness analyses in public health [156]. New and rigorous estimates

of the cost-effectiveness thresholds for low- and middle-income countries suggested that these thresholds usually are below 1 GDP per capita [155–158]. Therefore, the identified health economics studies in Central America using the WHO thresholds could be doing more harm than good in the population's health.

4.2 Trend and Extent of Health Economic Evidence in Central America

There was a paucity of studies published between 2001 and 2009. During this time frame, no HTA agency was functioning in the region. From 2010 onward the number of studies increased, and a large proportion of the studies were published as abstracts in the ISPOR conference proceedings. The absolute number of HEE and BIA studies per country in Central America highlighted that health economics as a field of research is at an early stage of development. For instance, when compared to other LMICs, the number of HEE studies per-country in Central America fall below those found individually in Brazil (n = 535) [32], Mexico (n = 122) [159], India (n = 104) [31], Colombia (n = 48) [29], South Africa (n = 45) [27] and Thailand (n = 39) [23], although the output is quite similar to those found in Vietnam (n = 26) [30], Zimbabwe (n = 26) [24] or Bangladesh (n = 12) [26]. Manyfold factors may explain the scarcity of health economics research in Central American countries. Although initial steps of institutionalisation and building HTA capacity have started in most of the Central American countries, the institutionalisation of the decision-making process, informed by HEE evidence, is still missing. A key element to increasing the demand for health economics research is to create an explicit link between economic evaluation and health decision making. Ideally, a legal framework must underpin this link. Moreover, the legal framework should define what type of economic evidence needs to be presented and define who can commission these studies. These conditions will provide fertile ground to produce more economic evidence to support informed decision-making in health.

We found that some health areas had a low volume of research when compared to their burden of disease in Central America. These findings highlight two points. First, for some countries (if not all), the number of studies is quite small. Consequently, there is not a clear pattern in the relationship between the burden of disease and the volume of studies. For instance, in Belize we only found four studies, which may make it difficult to find a defined pattern. Second, it could be that the development and introduction of health technologies follows the needs of the countries with the biggest market opportunities. Usually, the market's opportunities are concentrated in high-income countries [160].

4.3 Quality of Reporting Economic Evidence In Central America

First of all, it is important to recognise that the quality of reporting economic evidence depends on whether the study is published as an abstract or as a journal article. Abstracts lack detailed information due to word constraints, which prevents an objective assessment of the quality of reporting. Considering this, the limitations of the studies are mainly focused on those published as journal articles.

For HEE studies, major limitations for reporting concern inadequately reporting the economic inputs, the outcomes and the uncertainty measurements of the findings. Most of the limitations described in this review were also found in previous HEE studies conducted in Colombia [29], South Africa [27], India [31] and Vietnam [30]. We found that studies with the involvement of international authors (those who were non-local authors) had, on average, higher reporting quality in comparison to those without international authors. The findings could suggest the need to bring trained professionals into the health-sector analysis and the potential of international collaborations in health economics to build local-level technical capacity. On the other hand, we found that almost two-thirds of the studies (68.8%) did not report the use of methodological/reporting guidelines for HEEs. The quality of reporting would be improved and the existing technical limitations would be addressed through reinforcing the use of those reporting guidelines, including those translated into Spanish such as the 2022 CHEERS guideline [161]. Promoting adherence to the guidelines is needed to achieve high reporting standards, to increase the credibility and reproducibility of HEE studies and to improve their usefulness in health decision-making.

According to the HEE guidelines [48, 162], the societal perspective must be chosen to capture all the relevant costs associated with a healthcare intervention. However, our review showed that only one-fifth of the included HEE studies adopted the societal perspective. As the societal perspective reflects the out-of-pocket expenditure (OOP) of patients, it is important to prioritise the societal perspective analysis in future studies to capture all the impact of the health intervention in a society as a whole. This is particularly relevant in Central America where health systems are still primarily financed through OOP [163]. OOP reflects the total costs of healthcare when patients are attended to in the private sector, and reflects the partial costs when care is sought in the subsidised public health sector.

For the identified BIA studies, the quality of reporting was considered acceptable. This quality of reporting was mainly compromised where studies failed to provide the model framework, describe the cost analysis approach, and provide the source of the market shares where applicable. The first and second limitation may be addressed by

adhering to the guidelines for BIA studies [44, 45]. None of the BIAs included in this review reported the use of any research guidelines. In order to increase the quality of reporting, the use of the guidelines is highly recommended. For the latter limitation, the magnitude of such a problem has been previously described in a review of European BIA studies [34]. For example, the market share assumptions from panel experts are a key element that some BIAs fail to report. These limitations made it difficult to provide verifiable and acceptable reporting evidence for local decision makers. This is of special concern for those BIAs that are intended to be used as evidence to support the pricing negotiation policies or reimbursement policies for new technologies. It is strongly advised that researchers should provide the source of the parameters used in the budget impact models to allow readers and reviewers to check the quality of the reporting information as well as the validity of the assumptions made.

4.4 Implications for Public Health and Policy Decision-Making

Ministries of health need to manage the economic burden of healthcare and attain financial sustainability based on evidence-based policy-making. Despite the advances in HTA in the Central American region, the current base of economic evidence needs to be strengthened to feed into sound policy making. In addition, the demand for health economics studies should be aligned with the local epidemiological context. For instance, this review highlights that there is a need to promote the commission of the HEE and BIA studies in other chronic diseases such as diabetes, chronic kidney diseases or mental health. These diseases have a relatively high disease burden in Central America, and previous research has found that they accounted had a high economic toll in other countries [164–168]. Identifying these health areas as being of high importance to be analysed through the economic lens in the short term, will increase the government funding as well as boost the advocacy for use of such evidence by stakeholders. The non-governmental organisations (NGOs) involved in delivering healthcare services can also be potential audiences that could contribute to the use of economic evidence in health and healthcare. NGOs may use this evidence to recruit financial aid from international funding to support their expansion.

4.5 Limitations

This review has several limitations. The inclusion of only published studies (journal articles and conference abstracts) may have introduced publication bias [169], meaning that academic theses, government reports, pharmaceutical company reports, or studies in the form of consultancies and commissioned for private companies were not retrieved. This is certainly true for those health economics studies carried out as a government report and presented directly to policy makers instead of being submitted to scientific journals. Furthermore, for the quality of reporting of HEE studies we used the instrument developed by La Torre and colleagues [43]. We acknowledge that this instrument has limitations. For instance, the validation of the system of weights assigned by the consensus of experts should be monitored in order to assess its reliability. A comprehensive assessment of the methodological quality of the studies is far beyond the scope of this review but sets out a path for future research. The same is true when we assessed the quality of reporting of BIA studies. In addition, we acknowledge that for some studies it was difficult to rule out selection bias or disagreement between criteria in the reviewers. To minimise this bias, we used pre-defined inclusion criteria, and ongoing discussions between researchers were held throughout the review process.

5 Conclusion

In Central America the production of health economic research is sparse and needs to consider the local population's health needs and adhere to the reporting guidelines to improve its usefulness in health decision-making.

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Declarations

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Consent to participate Not applicable.

Consent for publication Not applicable.

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