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The economic burden of ischaemic heart diseases on health systems: a systematic review

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ABSTRACT

Introduction There is a dearth of evidence regarding the global economic burden of ischaemic heart diseases (IHDs). This systematic review aims to synthesise national-level studies worldwide quantifying the economic burden of IHDs from a provider's perspective.

Methods We searched PubMed, Embase, Cochrane, DARE and EconLit databases from 1 January 2000 to 29 June 2022. We included observational, cost-of-illness and economic modelling studies reporting direct healthcare cost data for IHDs at the national level. At least two reviewers independently screened titles and abstracts and full texts, extracted data and assessed quality using a seven-question assessment tool. We synthesised findings by country, focusing on three key economic estimates: total annual costs of IHDs, costs of managing acute IHD episodes and chronic IHD care. We correlated these costs with country-specific macroeconomic measures and disease burden.

Results We included 65 national-level studies conducted in 21 countries worldwide, with a majority in high-income countries. The median direct healthcare cost per episode of IHDs was 8062 Int$ 2019 (IQR: 5770–9580), and the median direct healthcare cost of IHDs per patient-year was 10 064 Int$ 2019 (IQR: 7619–14 818). These estimates positively correlated with country-specific macroeconomic and DALY measures.

Conclusion IHDs impose a substantial economic burden on health systems globally. Economic costs in countries exceed per capita public health expenditure, primarily driven by acute episodes. National-level data were available for only 21 countries, and none from low-middle-income and low-income countries. Economic costs of IHDs need to be quantified to inform resource allocation decisions at national and global levels.

PROSPERO REGISTRATION NUMBER
CRD42022337577.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There was the absence of any published or registered systematic review on the global economic burden of ischaemic heart diseases (IHDs). Previous systematic and non-systematic reviews on the economic burden have predominantly focused on cardiovascular diseases in general, with a primary emphasis on low-income and middle-income countries (LMICs) or specific subpopulations like those with diabetes. As a result, a significant gap exists in our understanding of the global and country-level economic burden of IHDs.

WHAT THIS STUDY ADDS

⇒ The economic burden of IHDs is substantial and exceeds the per capita public current health expenditure worldwide, particularly in LMICs; this burden is primarily driven by the costs associated with acute episodes of IHDs rather than the chronic care nature of the condition.

⇒ The relatively lower cost burdens observed in post-acute IHD care may suggest the potential underutilisation of cardiac rehabilitation programmes for patients in the post-acute phase of IHDs on a global scale.

⇒ Despite IHDs being the leading cause of mortality and morbidity globally, only 21 countries had national-level data on the direct healthcare cost of IHDs, and none of these data originated from low-middle-income and low-income countries.

INTRODUCTION

Cardiovascular diseases (CVDs) pose a major challenge to health systems, with the global prevalence nearly doubling from 271 million people in 1990 to 523 million in 2019.[1] As the leading cause of mortality worldwide, CVDs were responsible for approximately 17.9–18.6 million deaths in 2019, accounting for nearly one-third of all deaths globally.[2 3] Beyond the devastating loss of lives, CVDs impose a substantial burden on health systems and countries. Their global economic burden is substantial, estimated at US$863 billion in 2010.[4 5] Projections indicate that this burden will likely surpass US$1044 billion by 2030.[4] However, these estimates and projections date back to 2010.

The four major contributors to the substantial disease burden associated with

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ We advocate for enhancing each country's existing national routine health information systems to comprehensively capture a wide range of healthcare services and health data, which will facilitate national-level economic burden studies of IHDs. To support meaningful and in-depth analyses, it would be beneficial to ensure adequate access to these systems, along with appropriate financial resources and expertise.

⇒ At the national level, countries could consider strengthening or implementing cost and outcome measurement systems, such as national or regional registries. These systems will enable the collection of data from providers necessary for calculating IHD costs.

⇒ At the global or regional level, multilateral institutions, such as the WHO, or intergovernmental bodies, such as the Organisation for Economic Co-operation and Development (OECD), could integrate IHD cost data in their existing data analytical platforms, such as OECD.Stat, to promote country reporting and facilitate benchmarking and comparison.

⇒ Policy-makers should consider prioritising primary prevention strategies for IHDs and emphasising long-term cardiac rehabilitation programmes to mitigate the development of acute episodes of IHDs and prevent recurrent cardiovascular events.

⇒ Our findings raise concerns regarding the global and national research priorities and resource constraints for conducting nationally representative economic burden research on IHDs, especially in LMICs.

CVDs are ischaemic heart diseases (IHDs), stroke, hypertension and heart failure. Together, these four conditions constitute approximately 82% of the global burden of CVDs annually.[3 4] Among them, IHDs stand out as the leading cause of morbidity and mortality from CVDs.[3 4] In 2019, IHDs accounted for nearly half of all CVD-related deaths worldwide,[3] with 182 million Disability-Adjusted Life Years (DALYs) lost.[1]

Numerous studies have examined the disease burden of IHDs worldwide; however, there is a considerable scarcity of literature concerning its economic burden worldwide.[6] Earlier systematic and non-systematic reviews have primarily focused on CVDs in general and mainly focused on low-income and middle-income countries (LMICs), or specific subpopulations, such as those with diabetes.[7–9] Hence, there is a specific gap in our understanding of the economic burden of IHDs globally and at the country level.

The purpose of this systematic review is to provide an analysis and synthesis of the studies that have quantified the economic burden of IHDs from a provider perspective globally. This perspective is selected because it is widely studied, quantifiable, transparent and concrete. Our review focuses on national-level studies and includes the most representative economic estimates at a country level. We also analyse the correlations between estimates of economic cost of IHDs and selected macroeconomic and disease burden measures.

METHODS

We registered the systematic review with PROSPERO (registration number: CRD42022337577). We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 Statement.[10]

Searches

We designed our own search strategies using medical subject headings and keywords. We searched five databases: PubMed, Embase, CENTRAL in The Cochrane Library, DARE and EconLit (see online supplemental method 1 for the full search strategies). For high-income countries, as classified by the World Bank,[11] we searched from 2000 to 29 June 2022. However, for upper-middle-income, lower-middle-income and low-income countries categories, our search covered the period from June 2015 to 29 June 2022. Search results before June 2015 were obtained from the references cited by the Gheorghe *et al* study.[7] We did not apply language restrictions.

Eligibility criteria

We developed our own eligibility criteria for the studies to be included, as follows:

Type of study

We included any primary studies that reported primary data on economic burden estimates for IHDs, including cost-of-illness studies, economic modelling studies and studies of observational design that include a cost collection component or report any microeconomic outcomes (e.g., direct cost of IHDs per episode or per patient-year) or macroeconomic outcomes (e.g., cost of IHDs as a percentage of gross domestic products (%GDP)) expressed in monetary units. Regarding the study scope, eligible studies had to be conducted at the national level, either through a representative sampling of healthcare facilities or through modelling. We excluded economic evaluation studies, systematic reviews, non-systematic reviews and studies that solely investigated the cost of drugs or treatment interventions, such as coronary artery bypass grafting.

Type of condition

Our condition of interest was IHDs, including non-ST-segment elevation myocardial infarction (NSTEMI), STEMI, unspecified myocardial infarction (MI) and unstable angina. We focused on both acute events (acute episodes) and chronic care for the management of the disease. We excluded studies that focused on unspecified angina pectoris.

Outcomes

We included studies that estimated the economic burden of IHDs from a provider perspective. This perspective is defined as the costs incurred by healthcare providers

(e.g., hospitals or primary healthcare facilities), regardless of who ultimately pays for these costs (e.g., public or private insurance funds, Ministries of Health or patients and their families). Examples of economic estimates of interest included the total annual healthcare cost of IHD, the direct healthcare cost of IHD per episode and the direct healthcare cost of IHD per patient over a defined period. We focused on these measures because they are widely studied, quantifiable, transparent and concrete. We excluded studies that solely investigated non-monetary microeconomic outcomes, for example, productive time lost due to illness, and studies that reported the economic burden incorporating both direct and indirect costs but did not provide sufficient information to separately quantify the direct healthcare costs of IHD.

Context

We focused on the global setting and categorised countries using the World Bank country classification by GDP per capita income level to guide our search strategy.[11]

Selection of studies

We used Covidence, an online software tool for managing systematic reviews, to manage all citations identified from the search.[12] After removing duplicates from the search results, five review authors (TR, MS, SG, ZD and KFL) worked independently to screen the titles and abstracts in duplicate. We classified each record as relevant or non-relevant for full-text review. Seven review authors (TR, CB, CR, MS, SG, ZD and KFL) independently reviewed full-text reports classified as relevant from the title and abstract screening in duplicate to determine the final eligibility. For search results of upper-middle-income, lower-middle-income and low-income countries before June 2015, we full-text screened included studies obtained from the study by Gheorghe *et al* against our eligibility criteria.[7] For studies excluded at the full-text screening stage, we documented the reason(s) for exclusion. We generated a study flow diagram, using PRISMA 2020 Statement guideline,[10] that described the identification of reviews (figure 1). At each stage of the screening process, we resolved disagreements through discussion.

Data extraction and quality assessment

We used Microsoft Excel to manage data extraction and quality assessment. We developed a new data extraction form covering data items related to methodological characteristics of studies and economic estimates. We adapted the quality assessment form developed by Gheorghe *et al*, who conducted a systematic review on a similar topic.[7] We chose this quality assessment tool for two primary reasons: (1) the current lack of a standard tool that comprehensively evaluates the quality of cost studies across various study designs and (2) the need to ensure consistency in quality evaluation across related systematic reviews. The quality assessment tool developed by Gheorghe *et al*[7] provides a structured framework for quality assessment that aligns with our study's objectives and eligibility criteria. It consisted of seven questions evaluating the robustness of study design in two key aspects: (1) the structure of the economic study, as inspired by the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Statement[13] and (2) if applicable, the design of the epidemiological study that was conducted in conjunction with the economic study. For each included study, one review author extracted all relevant data items and evaluated the included studies' quality, which was then verified by another review author. Any discrepancies were resolved through discussion.

Data analysis

We summarised and tabulated information on the characteristics of included studies, including general study information, study design and economic estimates. We analysed three economic burden estimates: (1) the total annual healthcare cost (Int$ 2019) of IHD; (2) the direct healthcare cost (Int$ 2019) of IHD per episode, which represented costs incurred during the acute episodes of IHD and (3) the direct healthcare cost (Int$ 2019) of IHD per patient over 1 year (patient-year), which represented costs incurred over a 1-year period (i.e., chronic care), encompassing the acute episode(s) of IHD and subsequent care, such as rehabilitation, ongoing monitoring and follow-up.

We narratively synthesised national-level estimates of the economic burden of IHD from the provider perspective for each country, using boxplots to demonstrate the distribution of each estimate across countries. For the total annual healthcare cost of IHD, we further categorised the country comparisons by population size. This approach is based on the rationale that the number of IHD patients in each country, which positively correlates with the country's population size, is a primary factor in calculating this estimate. Therefore, countries with larger populations generally have higher total healthcare costs for IHD. Additionally, we compared these estimates against macroeconomic measures, including GDP per capita in 2019 (Int$ 2019), per capita current health expenditure in 2019 (Int$ 2019), per capita public current health expenditure in 2019 (Int$ 2019) and a disease burden measure (ie, DALY of IHD). We also calculated correlation coefficients ('ρ') to determine the strength and direction of the linear relationship between the costs of IHD and the macroeconomic and disease burden measures. When more than one included study reported the same economic estimate for the same country, we selected the study that reported the most recent outcome year for analysis. Our justification for this choice was to capture the most current state of the economic burden of IHD.

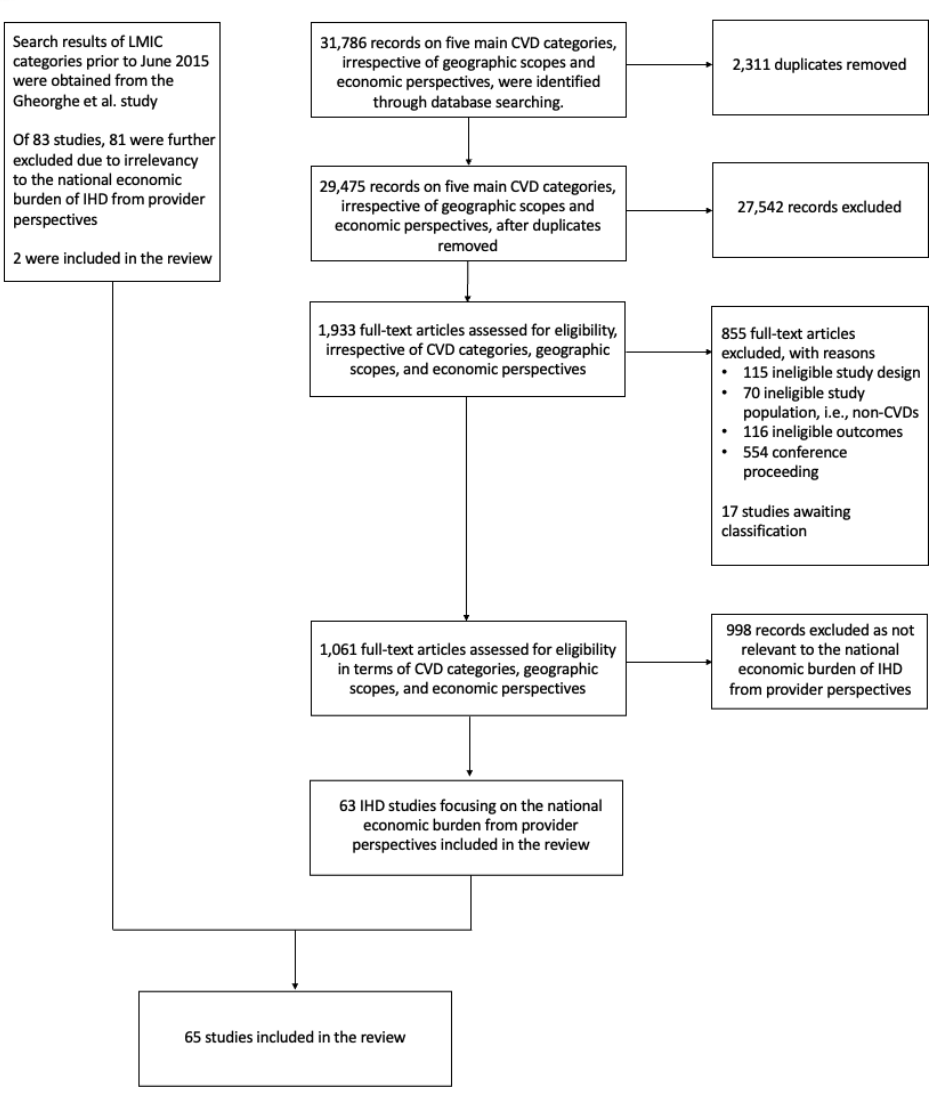

Figure 1 PRISMA flow diagram. CVD, cardiovascular disease; IHD, ischaemic heart disease; LMIC, low-income and middle-income country; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

We converted all IHD cost data to purchasing power parity (PPP)-adjusted US$ 2019 (Int$ 2019) using the Campbell and Cochrane Economics Methods Group Evidence for Policy and Practice Information and Coordination Centre cost converter.[14] In cases where the base year of the currency was not explicitly mentioned or could not be inferred from the manuscript, we assumed it to be the year preceding the publication of the paper. We obtained the macroeconomic measures (eg, GDP per capita) from the World Bank's Development Indicators[15] and the health financing data from the WHO's Global Health Expenditure database,[16] while we obtained the DALY data from the Global Burden of Disease Study 2019 (GBD 2019).[17] We did not plan to perform any quantitative syntheses or meta-analysis since we expected high heterogeneity across studies regarding setting, population and cost components included in measurements. We analysed data using Microsoft Excel and R Studio software.[18]

Patient and public involvement

Patients were not involved in the design or conduct of this systematic review.

RESULTS

Search results

The literature search on five main CVD categories (i.e., heart failure, hypertension, IHDs, stroke and unspecified CVDs), irrespective of geographical scope and economic perspective, yielded 31 786 records. After the removal of duplicates and excluding studies on the basis of their title and abstract or through full-text assessment, 63 articles were identified as eligible for inclusion in the review and 2 eligible studies[19 20] were further identified from the Gheorghe *et al* study,[7] resulting in a total of 65 included studies, reporting economic estimates for 21 different countries.

Study characteristics

Table 1 summarises the key characteristics of the 65 included studies that investigated the economic burden

Table 1 Characteristics of included studies (n=65)

Characteristics	No (%) of studies
Countries by income level according to the World Bank country classification	
High-income countries*[21–75]	55 (85)
Upper-middle-income countries†[19 20 76–83]	10 (15)
Lower-middle income countries	0 (0)
Low-income countries	0 (0)
Disease presentation	
Acute[19 23 24 27–31 33–35 38 41 47 48 53 55 56 62 63 65 69–73 75 80 81]	30 (46)
Chronic[25 32 42 51 52 59 60 64 68 76 78 82]	12 (19)
Both[20–22 26 36 37 39 40 43–46 49 50 54 57 58 61 66 67 74 77 79 83]	23 (35)
Healthcare setting	
Primary care only[25 38 42 59 64 68]	6 (9)
Secondary care only[19–23 27–32 35 45–50 53–57 62 63 66 74 76 77 80 81]	31 (48)
Tertiary care only[26 33 40 41 52 58 65 69–72 78 82]	13 (20)
Primary and secondary care[51 60]	2 (3)
Secondary and tertiary care[24 67 73 75]	4 (6)
Primary, secondary and tertiary care[34 36 37 39 44 61 79 83]	8 (12)
Not specified[43]	1 (2)
Type of payer	
Government[19–21 23 24 26 31 32 37 39–41 45 49–54 57 58 60 62–72 75–77 79–82]	40 (61)
Private insurance[22 34 48 59 61]	5 (8)
Both[25 27–30 33 35 36 38 42–44 46 47 55 56 73 74 78 83]	20 (31)
Study design	
Prospective cost study[33 51 61 68 73]	5 (8)
Retrospective cost study[21–23 25 26 30 32 36 37 39 41 42 46 47 49 52–54 62 63 66 67 80]	23 (35)
Database analysis[19 20 24 27–29 31 34 35 38 40 43–45 48 50 55 60 65 69–71 81 82]	24 (37)
Mathematical model[59 72 75 76]	4 (6)
Survey[77]	1 (2)
Cost-of-illness study[56–58 64 74 78 79 83]	8 (12)
Sources of data	
Disease incidence/prevalence data	
National database[20 22–33 35 37–45 47 49–58 60–66 69–82]	55 (84)
Private insurance database[46 48 68]	3 (5)
Other (eg, multiple databases, literature review, research database, hospital records, simulation results, unclear)[19 21 34 36 59 67 83]	7 (11)
Utilisation data	
National database[19 20 22–33 35 37 39–43 45 47 49 50 52–58 60–66 69–75 77 79–82]	52 (80)
Private insurance database[36 44 46 48 68]	5 (8)
Expert opinions[67]	1 (1)
Other (eg, multiple databases, literature review, research database, hospital records, simulation results, unclear)[21 34 38 59 76 78 83]	7 (11)
Cost data	
National database[20 22–33 35 37–43 45 47 49 50 52–58 60 61 63 64 66 68–75 79 81 82]	48 (74)
Private insurance database[36 44 46 48]	4 (6)
Hospital records[67 76 78 80]	4 (6)
Other (eg, multiple databases, literature review, expert opinions, research database, simulation results, unclear)[19 21 34 51 59 62 65 77 83]	9 (14)
Other characteristics—median (IQR)	
Median publication year (No. of studies=65)	2014 (2010–2018)
Median total number of participants (No. of studies=58)	101 705 (26 373–463 743)

*Australia, Belgium, Canada, France, Germany, Hong Kong, Italy, Japan, Netherlands, New Zealand, Slovenia, South Korea, Switzerland, Taiwan, UK and USA.
†Brazil, China, Iran, Thailand and Turkey.

of IHDs from a provider perspective in 21 different countries.[19–83] Of the 21 countries, 16 (76%) were classified as high-income countries, while the remaining 5 (24%) were classified as upper-middle-income countries. None of the countries were lower-middle-income or low-income.

Geographically, the largest portion of the included studies (30 studies, 46%) focused on the USA, followed by 5 studies (8%) from Brazil, and 3 studies (5%) each from Germany and the UK. Additional studies examined IHDs in Australia, Belgium, Canada, China, France, Hong Kong, Iran, Italy, Japan, Netherlands, New Zealand, Slovenia, South Korea, Switzerland, Taiwan and Thailand.

Regarding disease presentation, 30 studies (46%) examined acute episodes of IHDs, 12 (19%) focused on chronic care and 23 (35%) covered both acute episodes and chronic care for IHDs.

Regarding healthcare settings, 6 studies (9%) assessed the economic burden of IHDs in primary healthcare settings, while 31 studies (48%) focused on secondary healthcare, 13 studies (20%) on tertiary healthcare and another 14 (21%) on multiple healthcare settings. There was one study where the healthcare setting was not specified.

Regarding the payer of IHD care, the costs of IHDs were covered by different types of payers: government

(40 studies, 61%), private insurance (5 studies, 8%) and both (20 studies, 31%).

The included studies used various research designs, including 24 database analyses (37%), 23 retrospective cost studies (35%), 8 cost-of-illness studies (12%), 5 prospective cost studies (8%), 4 mathematical modelling studies (6%) and 1 survey (2%). The definition of each study design has been described in the Gheorghe *et al* study.[7] Most studies obtained their data from national databases, with a smaller proportion using private insurance databases and other data sources (e.g., hospital records, literature reviews and expert opinions).

The median total number of study participants in each included study was 101 705, with an IQR from 26 373 to 463 743. The median publication year was 2014, with an IQR from 2010 to 2018. For detailed characteristics of the included studies, refer to online supplemental table 1.

Economic burden

We selected 29 included studies of 21 countries that reported the most recent year for each outcome of interest for analysis.[20 33 39 50 51 54–56 58–60 62–67 69 70 72–80 83] Of all 29 studies, 14 studies from 14 different countries were analysed for the total annual direct healthcare costs,[39 56 58–60 64 69 72 74–76 78 79 83] 11 studies from 11 different countries were analysed for the direct healthcare costs of IHDs per episode[20 33 54 55 62 65 67 70 73 77 80] and 7 studies from 7 different countries were analysed for the direct healthcare costs of IHDs per patient-year.[50 51 60 63 66 67 77]

Economic burden of IHDs from provider perspective

Figure 2 presents the total annual direct healthcare costs of IHDs (Int$ 2019) while figures 3 and 4 present the direct healthcare costs of IHDs per episode and per patient-year (Int$ 2019) across countries with data available worldwide.[20 33 39 50 51 54–56 58–60 62–67 69 70 72–80 83] Among all countries globally, the total annual direct healthcare costs of IHDs were investigated in 14 countries, with a median of 1588 million Int$ 2019 (IQR: 608–4947 Int$ 2019; figure 2).

Among the countries with relatively small population sizes (i.e., population size less than 20 million in 2019), the median total annual direct healthcare cost of IHDs was 2053 million Int$ 2019 (IQR: 303–4139 Int$ 2019), with the highest cost reported in New Zealand (5351 million Int$ 2019) and the lowest cost in Slovenia (98 million Int$ 2019), as shown in figure 2A.

Among the countries with medium population sizes (i.e., population size between 20 and 100 million in 2019), the median total annual direct healthcare cost of IHDs was 1323 million Int$ 2019 (IQR: 610–1588 Int$ 2019), with the highest cost reported in Turkey (3610 million Int$ 2019) and the lowest cost reported in Australia (59.14 million Int$ 2019), as shown in figure 2B.

Among the three countries with relatively large population sizes (i.e., population size greater than 100 million in 2019), the median total annual direct healthcare cost of IHDs was 87 220 million Int$ 2019 (IQR: 48 269–205 695 Int$ 2019), with the highest cost reported in China (324 170 million Int$ 2019), followed by the USA (87 220 million Int$ 2019) and Brazil (9319 million Int$ 2019), as shown in figure 2C.

Regarding the economic burden of IHDs from a provider perspective in managing acute episodes of IHD (figure 3), studies conducted in 11 countries investigated the direct healthcare costs of IHDs per episode, with a median of 8062 Int$ 2019 (IQR: 5770–9580 Int$ 2019). The direct healthcare costs of IHDs per episode were highest in the USA (20 901 Int$ 2019), followed by Germany (11 843 Int$ 2019) and Switzerland (10 146 Int$ 2019). They were lowest in Brazil (2072 Int$ 2019), followed by Turkey (4117 Int$ 2019) and Italy (4727 Int$ 2019)

In terms of the economic burden of IHDs from a provider perspective for providing chronic care (figure 4), studies conducted in seven countries investigated the direct healthcare costs of IHDs per patient-year, with a median of 10 064 Int$ 2019 (IQR: 7619–14 818 Int$ 2019). The direct healthcare costs of IHDs per patient-year were highest in the USA (21 086 Int$ 2019), followed by Germany (18 378 Int$ 2019) and the UK (11 258 Int$ 2019). They were lowest in Turkey (5028 Int$ 2019), followed by New Zealand (7339 Int$ 2019) and Japan (7899 Int$ 2019). For more details on the total annual direct healthcare cost of IHDs and the direct healthcare cost of IHDs per episode and per patient-year by country, refer to online supplemental table 2 and 3, respectively.

Economic burden of IHDs from a provider perspective and its correlation with macroeconomic measures

Figure 5A1,B1 show positive correlations between the direct healthcare cost of IHDs per episode and per patient-year and GDP per capita, suggesting that countries with higher GDP per capita tended to have higher direct healthcare costs associated with IHDs both in management of acute and chronic phases of the condition.

However, in the management of acute episodes (figure 5B1), Thailand reported relatively higher cost per episode of care for IHDs (figure 5B1) when compared with other countries with similar GDP per capita levels, that is, Brazil (figure 5B1) and Turkey (figure 5B1). The cost per episode of care in Thailand was as high as that reported in Taiwan (figure 5B1), which had almost three times greater GDP per capita compared with Thailand. Among European countries, Germany reported relatively higher costs (figure 5B1) and Italy reported relatively lower costs (figure 5B1) associated with IHDs when compared with other European countries with similar economic conditions, including Belgium, France and the Netherlands. Switzerland had the highest GDP per capita but exhibited costs similar to those in Belgium, France and Germany, where the GDP per capita was half as much (figure 5B1).

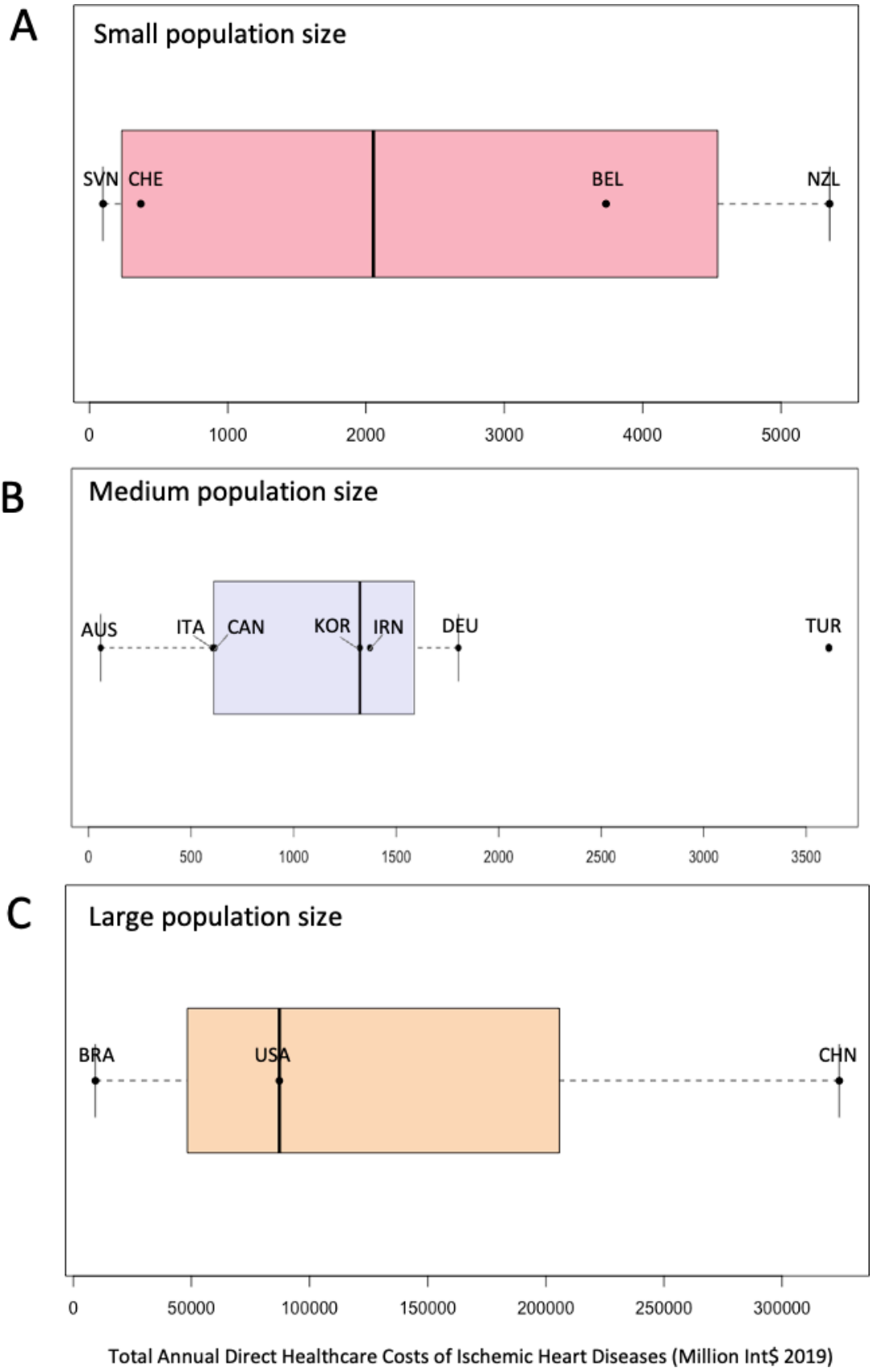

Figure 2 Boxplots of total annual direct healthcare costs of ischaemic heart diseases (n=14) for country groups of population size less than 20 million, between 20 and 100 million and greater than 100 million. AUS, Australia; BEL, Belgium; BRA, Brazil; CAN, Canada; CHE, Switzerland; CHN, China; DEU, Germany; IRN, Iran; ITA, Italy; KOR, South Korea; NZL, New Zealand; SVN, Slovenia; TUR, Turkey; USA, United States.

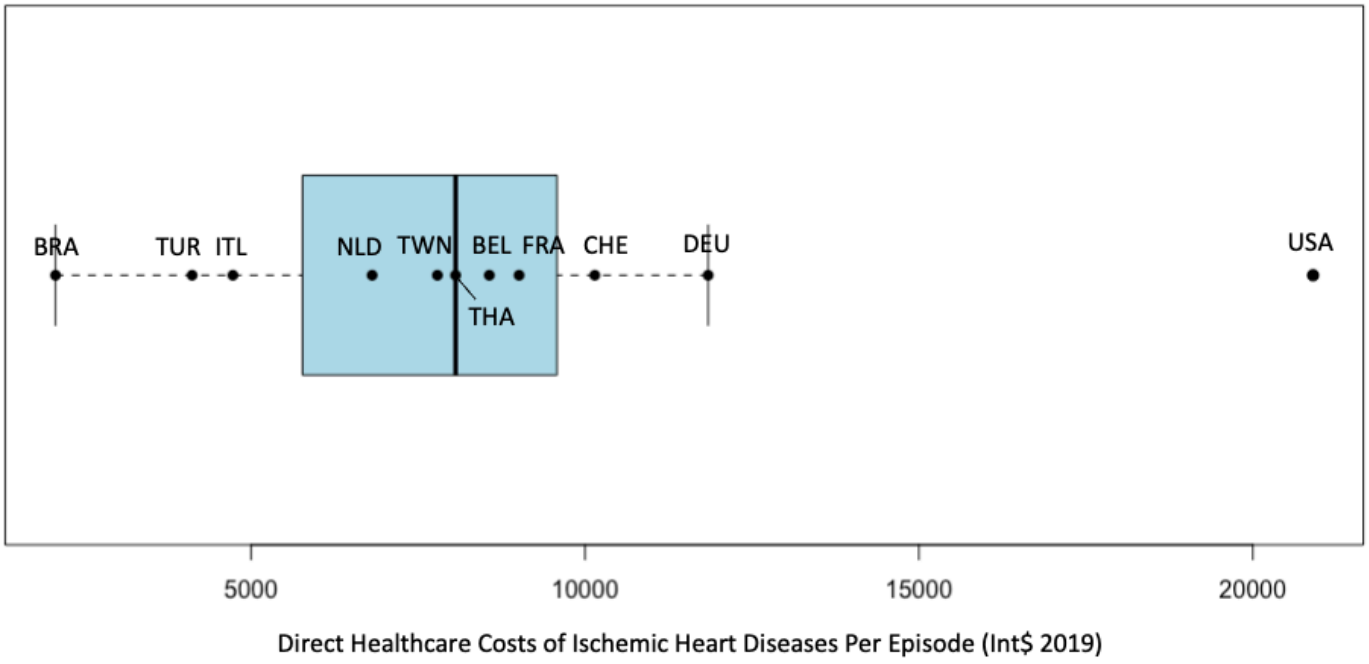

Figure 3 Boxplot of direct healthcare costs of ischaemic heart diseases per episode of care for 11 countries. BRA, Brazil; BEL, Belgium; CHE, Switzerland; DEU, Germany; FRA, France; ITA, Italy; NLD, Netherlands; THA, Thailand; TUR, Turkey; TWN, Taiwan; USA, United States.

Although the USA had a GDP per capita that was 18% less than Switzerland, it exhibited the highest costs (figure 5B1) among all countries with available data. Likewise, when managing chronic phase of IHDs (figure 5A1), Germany reported relatively higher costs (figure 5A1), compared with other countries in similar GDP per capita income groups, such as Hong Kong (figure 5A1) and the UK (figure 5A1).

Similar positive trends were observed for the relationships between the direct healthcare costs of IHDs per episode and per patient-year versus per capita current health expenditure and per capita public current health expenditure (figure 5A2, A3 and B2, B3). Regarding the strength of associations, a correlation coefficient for the per capita current health expenditure was higher compared with the

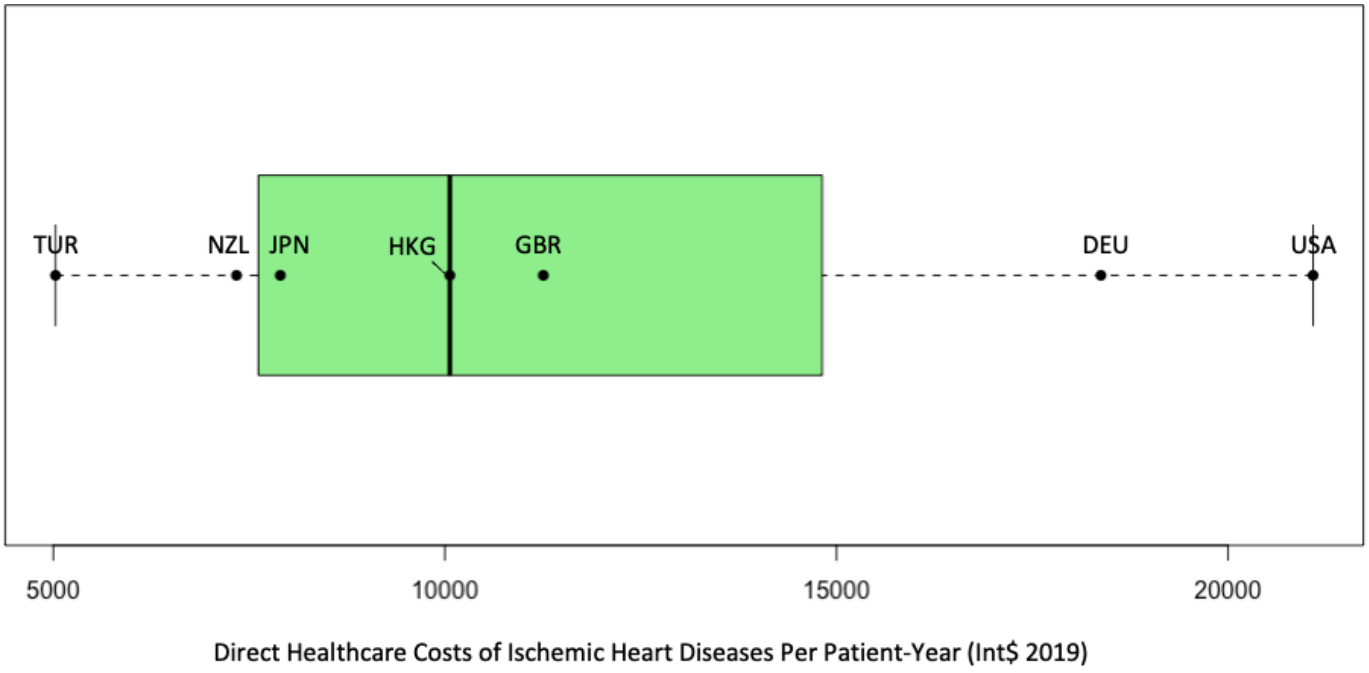

Figure 4 Boxplot of direct healthcare costs of ischaemic heart diseases per patient-year for seven countries. DEU, Germany; GBR, United Kingdom; HKG, Hong Kong; JPN, Japan; NZL, New Zealand; TUR, Turkey; USA, United States.

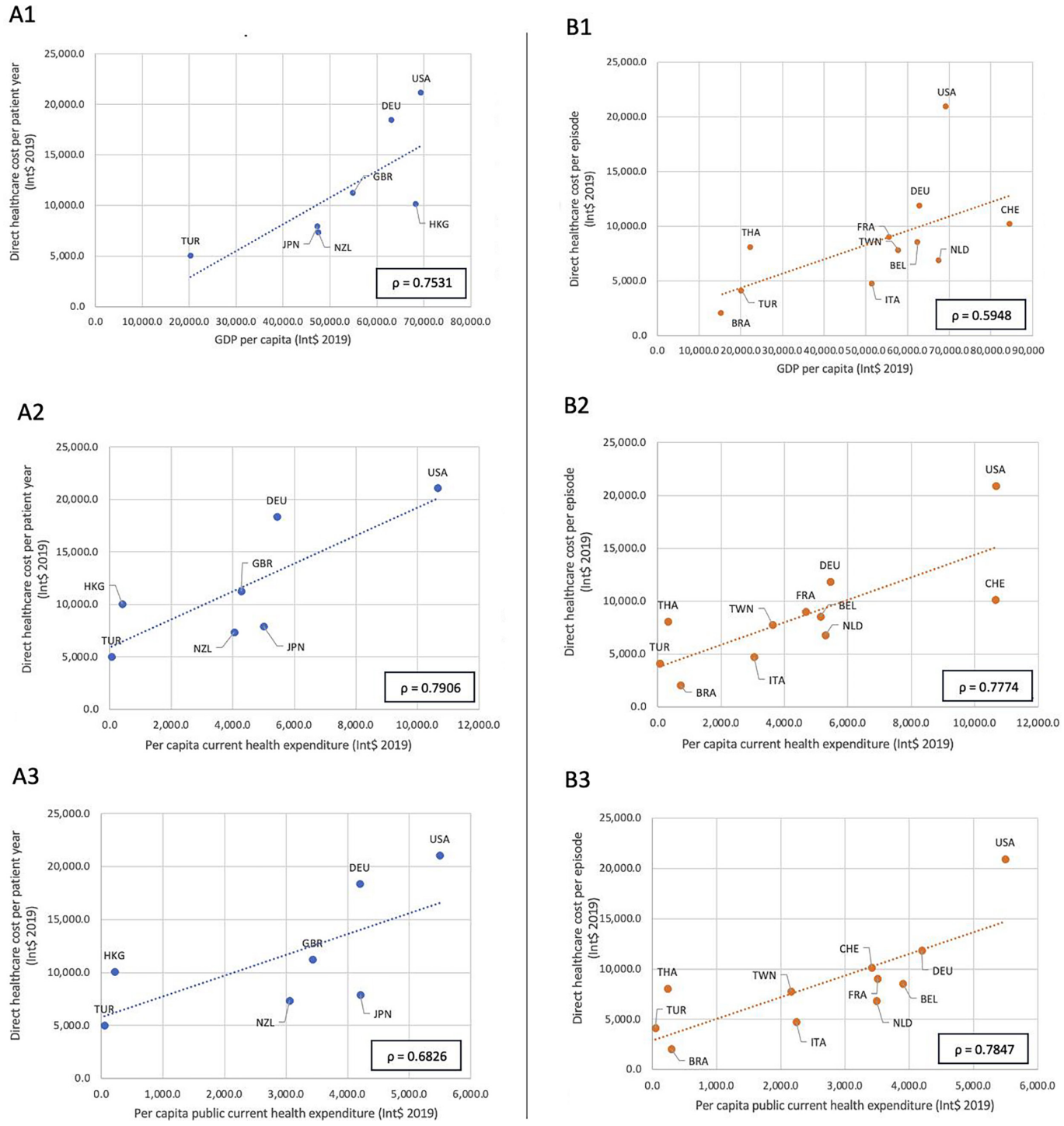

Figure 5 Scatter plots of the direct healthcare cost per episode and per patient-year against macroeconomic measures (GDP per capita, per capita current health expenditure, and per capita public current health expenditure) by country. BEL, Belgium; BRA, Brazil; CHE, Switzerland; DEU, Germany; FRA, France; GBR, United Kingdom; HKG, Hong Kong; ITA, Italy; JPN, Japan; NLD, Netherlands; NZL, New Zealand; THA, Thailand; TUR, Turkey; TWN, Taiwan; USA, United States.

other two macroeconomic measures (GDP per capita and per capita public current health expenditure). Online supplemental table 3 provides more details on the direct healthcare costs of IHDs per episode and per patient-year, GDP per capita, per capita current health expenditure and per capita public current health expenditure by country.

Economic burden of IHDs from a provider perspective and its correlation with disease burden measures

Figure 6 shows a positive correlation between the direct healthcare costs of IHDs per episode and per patient-year and DALYs of IHDs. Countries with higher costs associated with IHDs for either acute episodes or chronic care tended to have higher

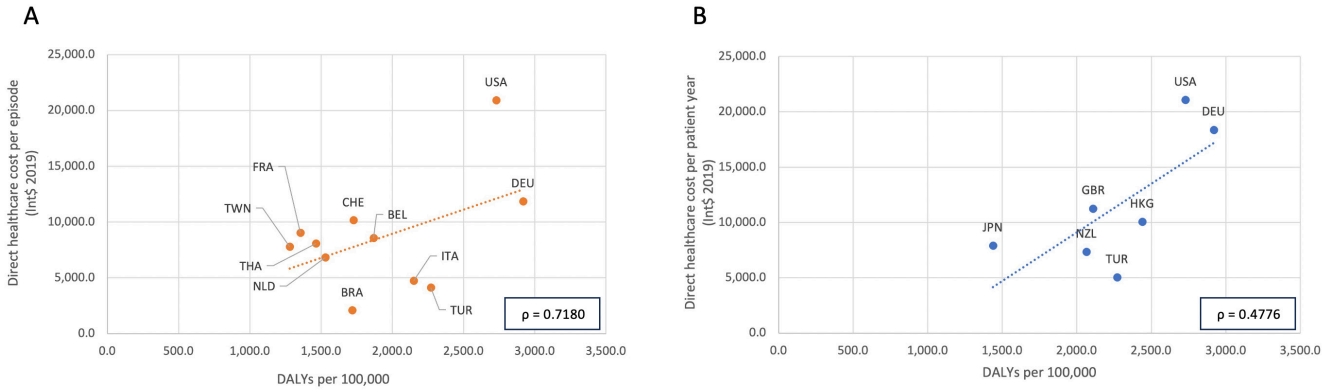

Figure 6 Scatter plots of the direct healthcare costs of ischaemic heart diseases (IHDs) per episode and per patient-year against DALYs of IHDs per 100 000 by country. BEL, Belgium; BRA, Brazil; CHE, Switzerland; DALY, Disability-Adjusted Life Years; DEU, Germany; FRA, France; GBR, United Kingdom; HKG, Hong Kong; ITA, Italy; JPN, Japan; NLD, Netherlands; NZL, New Zealand; THA, Thailand; TUR, Turkey; TWN, Taiwan; USA, United States.

disease burden of IHDs. However, there are some exceptions to this trend. In the management of acute episodes of IHD, some countries with relatively lower healthcare costs of IHDs, that is, Brazil and Italy, exhibit higher DALY values, while others with higher healthcare costs of IHD, that is, France, the Netherlands, Taiwan, Thailand and Switzerland, showed lower DALY values (figure 6A). In addition, although the USA exhibited twice the costs of IHDs as Germany, the disease burden of IHDs was similar between these two countries. In relation to chronic care, some countries with relatively lower healthcare costs of IHDs, for example, Turkey, exhibit higher DALY values, while others with higher healthcare costs, for example, Japan, show lower DALY values (figure 6B). For more details on the direct healthcare costs of IHDs per episode and per patient-year and DALYs of IHDs per 100 000 by country, refer to online supplemental table 3.

Quality assessment of the included studies

Table 2 summarises the quality assessment of included studies. In terms of the economic component of the study design, 60% (n=39) of the studies included an exploration of uncertainty and/or heterogeneity in the economic estimates, often by employing regression analysis. The data sources for expenditure, resource use and unit costs were clearly documented in nearly all of the studies (92%, n=60), and cost and productivity data were transparently presented in 82% (n=53) of them. However, of all the eligible studies, only a small proportion (11%, n=7) of them took into account productivity costs in their

Table 2 Quality assessment of included studies (n=65)

Quality criterion	Studies (n, %)		
	Yes	No	Unclear
Economic component			
Data sources for expenditure, resource use and unit costs were clearly explained	60 (92)	4 (6)	1 (2)
Cost and/or productivity data were transparently presented	53 (82)	12 (18)	0 (0)
Productivity costs were included	7 (11)	58 (89)	0 (0)
If productivity costs included, results were presented with and without productivity costs	6 (9)	1 (2)	n/a (90)
The analysis addressed uncertainty and/or heterogeneity	39 (60)	23 (35)	3 (5)
Epidemiological component			
The patient sampling method appropriate for deriving nationwide estimates of incidence/prevalence	49 (75)	5 (8)	0 (0); n/a 11 (17)
The source of incidence/prevalence data contributed to the study's internal validity	48 (74)	0 (0)	0 (0); n/a 17 (26)

n/a, not applicable.

estimations. In terms of epidemiological considerations, as we focused on national-level studies, all applicable included studies used nationally representative data sources for IHDs incidence/prevalence. Most of them (91%, n=49) used a sampling method that yielded results with generalisability. Refer to online supplemental table 4 for a detailed quality assessment for each included study.

DISCUSSION

Summary of findings

This systematic review provides the first synthesis of the published studies globally on the economic burden of IHDs from a provider perspective. We incorporated data from 65 national-level studies conducted in 21 countries.[19–83] More than 75% of these studies were conducted in high-income countries, while less than 25% were conducted in upper-middle-income countries.

Regarding acute episode of care, we found that the median direct healthcare cost of IHDs per episode was 8062 Int$ 2019 globally. The USA had the highest estimated cost (20 901 Int$ 2019), while Brazil had the lowest (2072 Int$ 2019). Regarding chronic care, the median direct healthcare cost of IHDs per patient-year was 10 064 Int$ 2019 globally. The USA again exhibited the highest estimated cost (21 086 Int$ 2019), with Turkey having the lowest (5028 Int$ 2019).

Our analysis found positive correlations between the direct healthcare costs of IHDs per episode and patient-year against macroeconomic measures, with the strongest correlation appearing to be with the per capita current health expenditure. Additionally, these costs showed positive correlations with DALYs of IHDs.

However, we observed some notable variations. For example, Germany displayed relatively higher costs in managing both acute episodes and chronic care of IHDs than other European countries with similar economic conditions. Despite having a relatively low disease burden of IHDs, Thailand tended to spend more on acute IHD care compared with other countries with similar levels of economic prosperity. The USA stood out for its disproportionately high costs for managing both acute episodes and chronic care of IHDs, while Switzerland exhibited relatively lower costs considering its level of economic prosperity.

Variations in the costs of IHD treatment across countries may be attributed to several factors. First, the proportion of general government health expenditure contributing to total current health expenditure may play a role. Countries with a higher proportion of government health expenditure are likely to allocate more funds to IHD care, potentially raising total treatment costs. Second, health system 'supply-side' factors such as differences in healthcare infrastructure and variations in the quality, efficiency and responsiveness of care processes may influence IHD treatment costs. For example, countries like Thailand that invest in secondary healthcare infrastructure, resulting in more advanced medical facilities and increased access to acute care, may have higher IHD treatment costs compared with those investing mainly in primary healthcare. Additionally, countries that invest heavily in advanced medical technology and procedures, or where the procurement of pharmaceuticals is more costly, such as Germany and the USA, are likely to have higher IHD treatment costs due to the higher costs associated with these advanced interventions. Third, the type of national health insurance schemes and provider payment mechanisms may influence IHD treatment costs. Countries with privately funded insurance and fee-for-service models, such as the USA, tend to have higher IHD costs compared with those with publicly funded systems and different payment models. Lastly, differences in risk factors among populations studied across countries may impact IHD care costs. Studies focusing on participants with multiple comorbidities will likely report higher costs than those involving healthier populations.

Added value of this study

The results of our systematic review shed light on a concerning finding. Despite IHDs being one of the leading causes of death worldwide,[6] we found that only 21 countries had national-level data on the direct cost of IHDs, and none of them were classified as lower-middle-income or low-income countries. Among the over 50 high-income countries worldwide,[11] only 16 (about 30%) reported the national-level economic burden of IHDs from a provider perspective. Furthermore, out of the over 40 upper-middle-income countries globally,[11] only 5 (about 12%) provided such estimates. These findings underscore the scarcity of evidence on nationally representative economic estimates of IHDs globally, which hinders our ability to understand the burden of IHDs and formulate appropriate policies to address this global health issue effectively.

The limited number of national-level studies investigating the direct healthcare costs of IHDs worldwide, especially LMICs, can be attributed to several factors. One possible explanation is the limitations of national routine health information systems and their capacity to collect and integrate comprehensive data on epidemiology, healthcare utilisation and costs related to IHDs.[84] Many countries, particularly LMICs, lack robust and standardised systems to capture and integrate such data at a national level. Even in countries with established RHIS, the comprehensiveness of collected data may be insufficient for accurately estimating the economic burden of IHDs, which requires a wide range of data, including direct healthcare costs, direct non-healthcare costs and indirect costs.[84–86] Resource constraints on conducting research and differing research priorities further contribute to the limited research on the economic impact of IHDs.

Second, we found that, globally, the median direct costs for managing acute episodes of IHDs were slightly lower than those for chronic IHD care, with a difference of 2002 Int$ 2019. These findings imply that the current

direct healthcare costs of IHDs primarily stem from the expenses incurred during the acute phase of the disease. One plausible explanation for the relatively higher costs observed in acute care settings could be the national-level resource prioritisation and management strategies during the acute phase of IHDs. Acute care settings generally prioritise immediate interventions and treatments to stabilise patients, which can result in substantial expenses. In contrast, the relatively lower costs observed in post-acute IHD phases may reflect either genuinely lower costs in post-acute care or the potential underutilisation of cardiac rehabilitation programmes for patients in the post-acute phase of IHDs.[87–90]

Lastly, we found that in all 12 countries worldwide with available data, regardless of their income level, direct healthcare costs of IHDs were high for acute episodes and for long-term care. In fact, these expenditures exceeded their per capita public current health expenditure by a considerable margin—the direct healthcare cost of acute episodes of IHDs surpassed the per capita public current health expenditure by a median factor of three, increasing to four when considering the long-term care basis. Additionally, the findings regarding Thailand and Turkey were of particular concern; these countries stood out with the highest ratio of direct healthcare cost of IHDs per episode to per capita public current health expenditure. In Thailand, the direct healthcare cost of IHDs in acute episodes exceeded the per capita public current health expenditure by a factor of 38. Similarly, in Turkey, this ratio was a factor of 13. These findings suggest a substantial financial strain on the healthcare systems in countries with lower economic prosperity, highlighting the urgent need for global efforts to prioritise and promote primary prevention of IHDs.

Strengths and limitations

Our findings align with previously published systematic and non-systematic reviews in general,[7–9] but we expanded on these findings in several ways. First, methodologically, unlike earlier reviews that focused primarily on LMICs, we broadened our eligibility criteria to include all countries globally. Besides, we focused specifically on IHDs, unlike earlier reviews that focused broadly on CVDs. Another critical differentiating aspect of our study was the specific focus on national-level studies. This approach allowed us to obtain the most nationally representative economic costs of IHDs and capture the overall distribution of evidence regarding the economic burden of IHDs from a provider perspective on a global scale. Another strength of our systematic review was that we further explored the differences in the direct healthcare costs between managing acute episodes of IHDs and chronic phase of IHDs, and compared them with relevant macroeconomic metrics and disease burden measured by DALY at a country level. These analyses aimed to better understand the costs of acute episodes and long-term care of IHD in different countries, by country income group, health expenditures (total and from government sources) and the disease burden of IHDs.

We acknowledged some limitations of our systematic review. First, we were unable to conduct meta-analyses or syntheses using all 65 included studies due to several methodological limitations in these studies and heterogeneities across them, including study methods, populations, definitions of IHD, comorbidities of patients, and, among others, healthcare setting for the study. Specifically, there was considerable variability in how economic estimates were derived, calculated and reported. Additionally, differences arose in population characteristics (eg, comorbidities, episodes of IHD and health system settings), the definition of IHD and the way IHD management was defined and costed. Additionally, many included studies lacked sufficient detail on these elements, limiting our ability to explore cost variations across and within countries. For example, several studies did not clearly specify the IHD conditions and interventions included in their cost estimates, the health system settings considered, whether comorbidities were accounted for, or how economic estimates were defined and calculated. Given these challenges, we opted for a narrative synthesis, prioritising studies that reported our prespecified outcomes of interest. To ensure consistency and minimise the influence of secular trends, we included the most recent study from each country eligible for our synthesis. Refer to online supplemental table 5 for the detailed outcome information and estimates reported by each included study.

Second, given the high heterogeneity in cost components, study populations, data collection methods and outcome time frames across studies, the economic estimates could be either overestimated or underestimated, and therefore, caution must be exercised when making cross-country comparisons. However, we tried to use the most nationally representative estimates reported in the included studies. Additionally, to facilitate cross-country comparisons, we converted all cost data to a standardised PPP-adjusted US$ 2019, with appropriate adjustments for inflation rates over time.[14] For included studies that did not provide a cost breakdown of their economic estimates, we assumed that their cost components consisted of hospital care, treatments/procedures, tests and supplies. Third, as our study focused exclusively on the direct healthcare costs of IHDs, representing the economic burden of IHDs solely from a provider perspective, it is worth noting that the overall economic burden of IHDs is much greater than these estimations, as there are other cost components that indirectly contribute to it, which were beyond the scope of this systematic review. These components include direct non-healthcare costs (eg, transportation and special dietary requirements) and indirect costs (eg, working time and income losses for both patients and caregivers).[9 91] Additionally, our focus on the national economic burden from the provider perspective may have resulted in the exclusion of some national-level studies that examine the economic

burden from other perspectives, such as that of patients. However, we anticipate that such exclusions are minimal due to the challenges and feasibility of obtaining nationally representative IHD cost data from other perspectives. Lastly, to facilitate cross-country comparisons regarding the direct healthcare costs of IHDs, we designed our eligibility criteria to exclude subnational studies and studies that reported the economic burden incorporating both direct and indirect costs but did not provide sufficient information to extract the direct healthcare costs of IHDs directly.

Policy and research implications

Our systematic review highlights several important considerations for policy-makers when addressing the economic burden of IHDs at a national level. First, given the limited evidence on the national-level economic burden of IHD in many countries, we advocate for enhancing each country's existing national routine health information systems, especially in LMICs.[85 92 93] Strengthening these systems will enable comprehensive national-level studies on the economic impact of IHDs so that policy-makers can make informed decisions. The improved health information systems should integrate a wide range of healthcare services information, including tests, medical supplies and medications while also incorporating individual patient data and health information. Standardised data collection protocols and regular quality assessments are essential to ensure the reliability of these systems.[86 94] Besides, appropriate monetary and non-monetary support, such as access to health information systems, financial resources and expertise, would be beneficial, especially in LMICs, to facilitate economic burden studies with meaningful and in-depth analyses. Second, investments should be directed towards primary prevention measures to mitigate the development of acute episodes of IHDs globally. By focusing on primary prevention, policy-makers can potentially reduce the incidence of IHDs, prevent costly acute episodes and lessen the economic strain on healthcare systems. Last, prioritising long-term care programmes for individuals with IHDs, such as cardiac rehabilitation, is essential to prevent recurrent cardiovascular events and further reduce exceeding costs over time. Evidence found that cardiac rehabilitation programmes, encompassing supervised exercise, lifestyle modifications and patient education, have effectively reduced the risk of subsequent cardiovascular events and improved patient outcomes.[95]

Our systematic review highlighted the need for future studies, both in HICs and LMICs, to (1) be reported in adherence to the CHEERS 2022 Statement,[13] (2) use a nationally representative database with an appropriate random sampling technique, or collect data from multiple study populations, areas and hospital levels if such a database is not available to ensure a representative sample, (3) include comprehensive cost components associated with healthcare services, encompassing hospitalisation, medication, outpatient consultations, treatments/procedures, tests, supplies, primary care services, emergency care services and rehabilitation care services and (4) explicitly report a cost breakdown and describe the method employed for cost calculation. Additionally, further studies should explore the economic burden and resource utilisation associated with specific components of IHD care, including acute events and chronic care, to gain deeper insights into the factors contributing to costs.

CONCLUSION

The economic burden of IHDs was substantial and surpassed the per capita public current health expenditure worldwide, primarily driven by the costs associated with the acute episodes of IHDs. Despite IHDs being the leading cause of mortality and morbidity globally,[6] only 21 countries had national-level data on the direct healthcare cost of IHDs, and none of these data originated from low-middle-income and low-income countries. It is essential for each country to promote the establishment of a nationally coordinated routine health information systems that facilitates national-level economic burden studies. Additionally, prioritising primary prevention strategies for IHDs and emphasising long-term cardiac rehabilitation programmes are essential steps in mitigating the global economic burden of IHDs.

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