A scoping review protocol on diagnostic and treatment costs of cardiovascular disease management in India [version 1; peer review: awaiting peer review]

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Abstract

Background: Cardiovascular disease (CVD) is a leading cause of mortality in India. Economic threats due to CVDs have surged, as diagnostic and treatment costs are out-of-pocket expenses. The increasing prevalence of CVDs in India is due to globalization, industrialization, aging, tobacco and alcohol consumption, diet, and sleep patterns. This scoping review provides a summary of the costs incurred in diagnosing and treating CVDs in India.

Methods: The JBI updated methodology aligned with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR) will guide this scoping review. Searches will be conducted on PubMed, Scopus, Cochrane Library, Embase, Econ Papers, and ProQuest databases. Google Scholar and Shodhganga will be used to search for relevant gray literature. Bibliographic mining will be performed to identify additional relevant studies. The literature published from 2000 onwards will be the primary focus. All direct and indirect costs for the diagnosis and treatment of CVDs across various levels of healthcare settings will be included. A two-stage independent screening, consisting of title and abstract screening, followed by full-text screening, will be conducted to identify eligible articles. Data will be extracted from full-text studies using a customized data extraction form. The results will be compiled and presented in the scoping review performed.

Ethics and dissemination: A conference presentation and scientific peer-reviewed journal publication will be the sources for disseminating the review results. This study does not require an ethics review because publicly available sources were used to retrieve data.
Keywords
cardiovascular disease, heart attack, hypertension, stroke, cost analysis, cost utility, cost effectiveness, cost, health care cost, direct cost, indirect cost, cost of illness, medical cost, non-medical cost

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Introduction
Non-communicable diseases (NCDs) are chronic in nature (Chronic diseases fact sheet, GACD), accounting for approximately 70% (41 million) of deaths globally (Noncommunicable diseases, WHO; Noncommunicable diseases Fact sheet, WHO). The global burden of NCDs increased briskly with a proportional rise attributed to cardiovascular diseases (CVDs) (Prabhakaran, Jeemon, and Roy, 2016) and would further increase to 55 million by 2030 if interventions were not opportune (Non-communicable Diseases, National Health Portal Of India). India recorded 63% of NCD fatalities in 2016, of which 27% were attributable to CVDs (Cardiovascular diseases in India, WHO). The World Health Organization (WHO) recommends a country-level target to reduce NCDs by 25% by 2025 and premature deaths by 33% by 2030. This can also prevent additional burden on healthcare costs and assist in attaining sustainable developmental goals (SDGs) (Cobiac and Scarborough, 2017).

The prevalence of CVDs was estimated to be 271 million worldwide in 1990, and this value doubled to 523 million in 2019. During the same period, the number of CVD-related deaths due to CVD increased from 12.1 million to 18.6 million (Roth et al., 2020).

WHO's action plan aspires to counter the CVD epidemic by encouraging research work, reducing, monitoring and modifying determinants and risk factors and integrating disease prevention programs and controlling local policies under global strategy for the prevention and control of NCDs (2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases, WHO). Low- and middle-income countries (LMICs) contributes to more than three-quarter of the world’s fatalities due to CVDs, which is attributed to insufficiency in primary healthcare services and the absence of robust universal health coverage (UHC) systems (CVDs Fact sheet, WHO). Out of the three-quarter deaths, around 40% fatalities are considered as premature. There is a need for sufficient data to support the likelihood that genetic, cultural, and environmental variations exist in the causes of CVDs by race and ethnicity. These variations should be considered when developing strategies for CVD prevention and treatment (Anand, Bradshaw, and Prabhakaran, 2020). Prominent unified factors, including economic, political, and cultural globalization, industrialization, and rapid urbanization are significant contributors to the increasing prevalence of CVDs in India. In addition, elevated levels of stress, inadequate physical activity, debilitated food and sleep patterns, heightened alcohol consumption, cigarette and tobacco smoking, and periodic sedentary lifestyles also pose significant risks (Prabhakaran and Yusuf, 2010). Lack of surveillance systems and proper and prompt diagnosis also contribute to the increasing prevalence of CVDs in India (Nag and Ghosh, 2013).

In 2016, the estimated prevalence of CVDs in India was 54.5 million cases. One in four deaths in India is attributed to CVDs, especially coronary artery disease and stroke, which accounts for greater than 80% of the burden of CVDs in India (Abdul-Aziz et al., 2019). Maximum number of cases are recorded in the Indian states of Kerala, Punjab, Tamil Nadu, Maharashtra, Andhra Pradesh, Himachal Pradesh, West Bengal, and Goa (Prabhakaran et al., 2018). Untimely mortality in India was 23.2 million in 1990, it increased by 59% to 37 million in 2010 because of CVDs (Prabhakaran, Jeemon, and Roy, 2016). Policy makers in India are hopeful that untimely deaths due to CVDs can be reduced by 25% with the implementation of national policies by 2025 (Prabhakaran et al., 2018). The number of deaths and number of hospitalizations due to CVDs in India was estimated at 1.4 million and 6.7 million in 2004 and it is expected to go up to 2.1 million and 10.9 million in 2021, respectively. Most of the hospitalized population belongs to the age group between 25 and 59 years (Srivastava and Mohanty, 2013). The estimated death rate attributed to CVDs in India was 256 per 1,00,000 population in 2019, which is more than double that of Japan, the country with the lowest death rate (77 per 1,00,000 population) (GBD Compare, IHME Viz Hub).

Every year, approximately 150 million people face financial emergencies owing to healthcare payments. Developing countries have meagre budgets for healthcare and are overly reliant on out-of-pocket health spending when compared to developed countries, which have a tax-funded health system or social health insurance schemes (Ezat Wan Puteh and Almualm, 2017). In 2010, the total cost related to medical care of CVDs was approximately USD 7.5 billion in India (Patel et al., 2020).

The estimated hospitalization cost for CVDs was INR 94 billion in 2004 and it is expected to project at INR 152 billion by 2021 (Prabhakaran et al., 2018). Prior studies on out-of-pocket expenditure (OOPE) in India have revealed that the hospitalization cost of CVDs could be five times higher in a private setting as opposed to a public one (Prinja et al., 2019). The estimated health care cost of CVDs was INR 8,483 (USD 114) in 2004–2005, which rose to INR 14,380 (USD 194) in 2011–2012 (Patel et al., 2020). Mean OOPE with respect to a specific disease and catastrophic health expenditure with relation to hospitalization in India was around INR 19,210 (the OOPE for heart diseases was approximately INR 40,947 (USD 552) in 2018 (Kastor and Mohanty, 2018). The poor and marginalized sections of the society are the predominant sections affected by OOPE for CVD treatment (Thakur et al., 2011).
To reduce the total economic burden, the Government of India (GOI) introduced Ayushman Bharat Yojana (ABY), a national health protection mission, in early 2018. This health insurance program is expected to benefit around half a billion poor and vulnerable families (Chowdhury and Mukherjee 2019, Macroscan). GOI is primarily focusing on addressing the increasing damage because of NCDs (Bhargava and Paul, 2020). A total of 150,000 Health and Wellness Centers are proposed to be established across India to give complete primary health-care services that are equivalent to the preeminent causes of huge burden of disease, including CVDs and other NCDs (AYUSHMAN BHARAT Comprehensive Primary Health Care through Health and Wellness Centers Operational Guidelines). Along with that it is expected to transform the grass root structure of primary, secondary, and tertiary health care systems in India (Verma, 2019). By ensuring access to quality health care and financial protection, India is perpetrated in achieving UHC for all by 2030 with ABY as an embryonic stride towards it (The long road to universal health coverage, NITI Aayog). Over the past few decades, CVDs have become a leading cause of mortality, causing a huge social and economic menace. The concept of UHC and insurance is growing constantly, but it is still a long way away to realize its potential, and to achieve this, there needs to be enormous stakeholder collaboration. Although research has been conducted on the costs of CVDs in India, a systematic or scoping review providing a comprehensive summary of the associated costs across various levels and sectors does not exist.

Thus, there is a need to synthesize evidence on this subject. To address this, a scoping review of peer-reviewed, non-peer-reviewed, and grey literature articles indicating the cost of CVDs is planned.

The objective of this review is to summarize the estimated costs associated with CVD care management in India with the available evidence and identify gaps in the literature. This study also aims to report the predominance of out-of-pocket spending and the economic burden of managing CVDs in India. This may aid policymakers in framing appropriate schemes to reduce OOPE and to encourage UHC. This study indirectly projects the potential impacts on inequalities in healthcare and strengthens the knowledge base for UHC in India.

**Methods**

**Protocol design**

Methods for this scoping review will follow the updated JBI methodology for scoping reviews (The Joanna Briggs Institute Reviewers’ Manual 2015 Methodology for JBI Scoping Reviews) along with Arksey and O’Malley’s scoping review methodology (Arksey and O’Malley, 2005) and Levac et al. (Levac, Colquhoun, and O’Brien, 2010) enhanced framework methods. The current protocol follows the Preferred Reporting Items for Systematic review and Meta-Analysis Protocol (PRISMA-P) (Moher et al., 2016) and the future scoping review will follow the PRISMA for Scoping Reviews (PRISMA-ScR) (Tricco et al., 2018). The scoping review will be carried out in five distinct stages:

1. Identification of the research question
2. Identifying relevant studies
3. Selection of eligible studies
4. Data extraction and charting
5. Collating, summarizing, and reporting the results

**Stage 1: Identification of the research question**

The broad question that directs this review is: what are the costs incurred for the diagnosis and treatment of CVDs in India? This review will elucidate relevant concepts by delineating and clarifying them, identifying research gaps, and reporting the most important evidence available to address and inform practice.

**Stage 2: Study identification**

**Inclusion criteria**

The literature published in English language from 2000 onwards will be considered in the scoping review. The population, concept, and context (PCC) frameworks will guide the inclusion and exclusion criteria for this review. Table 1 summarizes the PCC framework that we will use for study selection.
Population Studies that include participants/patients/individuals with borderline or established CVDs of any age in India will be included. As per the types given by WHO, the CVDs include cerebrovascular disease, coronary heart disease (CHD), congenital heart disease, peripheral vascular disease, deep vein thrombosis and pulmonary disease, rheumatic heart disease, their synonyms and commonly used terms will be included for the review (CVDs Fact sheet, WHO).

Concept The main concept of this review includes the direct and indirect costs incurred in the management of CVDs in India. This includes direct medical and non-medical costs, along with indirect costs. Direct medical costs include physician visits, emergency room services, and medications, while direct non-medical costs involve food, accommodation, and travel. Indirect costs include the loss of earnings, time, and productivity loss of both patients and their caregivers while seeking medical care (Ibrahim, Pozo-Martin, and Gilbert, 2015). In this review, the direct costs for common diagnostic programs such as blood pressure (BP), fasting lipoprotein profile, body mass index (BMI), blood glucose test, electrocardiogram (ECG), exercise stress test, echocardiogram, nuclear cardiac stress test, abdominal and carotid ultrasound, coronary angiogram, magnetic resonance image (MRI), and coronary computed tomography angiogram (CCTA) will be included (Diagnosing Heart Disease, Patient Education, UCSF Health), (Heart Procedures and Surgeries, American Heart Association), (Common medical tests to diagnose heart conditions, National Heart Foundation of Australia). Common treatment costs such as hospital costs, drug therapy, surgical procedures such as angioplasty, coronary artery bypass surgery (CABG), pacemakers, heart valve surgery, cardiomyoplasty, heart transplant, implantable cardioverter defibrillator, and rehabilitation costs will also be included, and many others will be premeditated and incorporated (Common medical tests to diagnose heart conditions, National Heart Foundation of Australia), (Coronary heart disease, Treatment, NHS), (Heart Procedures and Surgeries, American Heart Association). The diagnostic and treatment programs will be amended subsequently based on the studies. Other related costs will also be included and assessed. OOPE summarizes the cost borne by patients, in addition to the costs covered by a social security scheme or insurance coverage (Burden of out-of-pocket health expenditure, OECD iLibrary, 2009; Lorenzoni et al., 2015).

Context This scoping review aims to determine the economic burden of CVDs in India. Therefore, studies on all types of CVDs in India will be considered. This review will consider studies conducted in any clinical setting (e.g., inpatient, outpatient) or healthcare facilities (e.g., hospitals, health centers, nursing homes).

Types of evidence sources The eligible studies include case-control studies, cohort studies, cross-sectional studies, randomized control trials (RCTs), non-RCTs, before-and-after studies, qualitative and quantitative studies, conference papers, and peer and non-peer review studies. Letters to the editor, editorials, commentary perspectives, and reviews will be excluded. Studies on co-occurring diseases and CVDs will also be included. Studies on CVD prevention costs will get excluded, based on the initial scoping process.

Search strategy A comprehensive search strategy was developed to retrieve both published and unpublished studies. A primary search of PubMed (RRID:SCR_004846) was performed to identify relevant articles. The keywords used to describe pertinent articles are listed and used to develop a full PubMed search. The search strategy will be customized and modified, consisting of all keywords and index terms using Boolean operators for Scopus (RRID:SCR_022559), Cochrane Library.
Stage 3: Selection of eligible studies
After completion of the searches, all identified citations will be collated and transferred to Zotero (RRID:SCR_013784) version 5.0, and duplicates will be removed. In accordance with the eligibility criteria, a two-stage screening process comprising (1) title and abstract screening and (2) full-text screening will be performed. The inclusion and exclusion criteria based on the PCC framework are listed in Table 3. The two stages followed an identical process, where every article will be independently reviewed in teams of two, and the results will be documented in Microsoft Excel (RRID:SCR_016137) spreadsheets. In conclusion, relevant sources will be retrieved. The selected full text will be reviewed in detail based on the eligibility criteria. Further ambiguities regarding the eligibility of an article will be labelled and discussed with a subject expert or a senior reviewer. The reasons for the exclusion of studies will be reported and recorded at the full-text screening stage.

Stage 4: Data extraction and charting
Data from these studies will be independently extracted. A custom data extraction form developed by the research team, using Microsoft Excel as an abetting platform, will be used. The data extracted will capture study components such as author names, publication year, publication title, type of CVDs, intervention, target population, population excluded, study setting, study design, sample size, and diagnostic and treatment costs. The data extraction form will be pretested before implementation to ensure that it accurately captures imperative information. The necessary modifications will be made as required during the pilot process. A detailed explanation of all modifications will be provided in the scoping review. The resolution of the differences between the reviewers’ decisions will be discussed with a subject expert or a senior reviewer. Table 4 lists the preliminary data extraction template used in this study.
Table 3. Inclusion and exclusion criteria.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>Population</td>
<td>Participants of any age with borderline or established CVDs.</td>
<td>None.</td>
</tr>
<tr>
<td>Concept</td>
<td>All the studies involving cost associated with CVD management that includes direct or indirect costs and OOPE.</td>
<td>Prevention cost of CVDs.</td>
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<tr>
<td>Context</td>
<td>India</td>
<td>Studies outside India or studies with a focus on LMICs or South Asia, where the costs are not provided separately for India.</td>
</tr>
<tr>
<td>Types of evidence sources</td>
<td>Quantitative and qualitative study designs.</td>
<td>Reviews, letters to the editor, editorials, perspective papers, and commentaries.</td>
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</table>

CVD, cardiovascular disease; OOPE, out-of-pocket expenditure; LMIC, low- and middle-income countries.

Table 4. Data extraction form.

<table>
<thead>
<tr>
<th>Citation information</th>
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<tr>
<td>Title of the study</td>
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<tr>
<td>Authors</td>
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<td>Year of publication</td>
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<tr>
<td>Type and source of publication</td>
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<tr>
<td>Author affiliation</td>
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<td>Contact information</td>
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<td>Study characteristics</td>
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<td>Aim/Objectives of the study</td>
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<td>Study period</td>
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<td>Location (State where the study was conducted)</td>
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<td>Type of CVDs</td>
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<td>Type of economic evaluation</td>
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<td>Years of data collection</td>
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<td>Study design</td>
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<td>Target population</td>
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<td>Sample size</td>
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<td>Sampling method</td>
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<td>Study perspective</td>
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<td>Setting</td>
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<td>Data sources</td>
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<tr>
<td>Cost/economic outcomes measured</td>
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<td>Currency of cost</td>
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<tr>
<td>Key findings</td>
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CVD, cardiovascular disease.

Stage 5: Data analysis and reporting

A PRISMA flow diagram will be used to report the screening process (Moher et al., 2016). The flow diagram displays the decision-making process, as well as the outputs of the searches, elimination of duplicated citations, study selection, complete retrieval, additional bibliography mining, and presentation of the final summary. The results will be presented in
graphical, tabular, and detailed descriptive compositions that align with the purpose and scope of this review. Descriptive statistics, such as frequencies and central measures of tendency and plots indicating concepts or aspects of population characteristics, will be used to report the number of studies, type of CVDs, treatment and diagnostic procedures, study type and design, and costs incurred (direct and indirect) either in diagrammatic or tabular arrangements (Peters et al., 2015). Moreover, thematic and narrative approaches will also be incorporated for the analysis of quantitative and qualitative studies. The gaps and limitations in the current literature will be identified and summarized.

**Study status**
Currently the authors are performing searches on all the electronic databases mentioned.

**Discussion**
This scoping review will provide a comprehensive rundown of cost induction for CVD care management in India and raise awareness among patients, clinicians, decision makers, and third-party payers about the economic burden of such chronic diseases. Along with this, one suggestion is to grasp health inequalities and the high priority of UHC for the Indian population.

**Strengths and limitations of this study**
1. This is the first scoping evaluation of the costs associated with managing CVDs in India.

2. The current scoping study will employ eight electronic databases and tailored search terms that will be iteratively optimized to obtain as many relevant articles as possible. Grey literature will also be identified and synthesized.

3. An assessment of the quality of the articles included in the scoping review will not be performed because it is beyond the scope of the scoping review.

4. A scoping review was undertaken because the topic has not been extensively reviewed and the scope has a broader agreement.

**Ethics and dissemination**
This study does not require ethical approval because the information and data collected will be obtained from publicly available sources. Regarding dissemination activities, the full review will be presented at a relevant conference and submitted to a peer-reviewed scientific journal for publication to report the outcomes of the scoping review.

**Data availability**
**Underlying data**
No data are associated with this article.

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**References**


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