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Health system interventions for the cost containment of drugs used for cardiovascular diseases: A systematic review and exploration of how the results could be adapted to the Sri Lankan context

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ABSTRACT

Objectives: Cardiovascular disease (CVD) in low and middle-income countries (LMICs), accounts for over 80% of global CVD-related deaths. The high cost of drugs is a major concern in not of managing CVD. This study aimed to conduct a comprehensive review to identify interventions for cost containment of CVD drugs and use the intervention scalability assessment tool (ISAT) to examine the acceptability and application of relevant interventions in the Sri Lankan context, that can also be adaptable to other LMICs.

Methods: A systematic search across three databases (Medline, Web of Science and Embase) was completed to identify relevant health system interventions. The ISAT assessed the feasibility of adapting the identified interventions to Sri Lanka, using structured interviews with 25 Sri Lankan stakeholders representing five groups: health managers, cardiologists, pharmacists, nursing officers, and patients.

Results: The search yielded nine publications. Five were conducted on a national scale, while others were conducted at the regional levels. Seven were published in developed countries. The identified interventions were categorised into six intervention themes: Imposing a ceiling price or reference price; introduction of the polypill; introduction of volume price contract initiatives; prescribing generic and essential drugs; one intervention package including generics, essential medicine, 90-day drugs, and free delivery; and a second intervention package including discounts, rebates, cost-free medicine, and bundling. Assessment of six intervention themes revealed that methods of setting ceiling prices and controlling generic drug prescribing were the most popular, while other interventions were least popular.

Conclusions: The study provides a roadmap for future interventions based on successful scaling, emphasizing the importance of understanding contextual variables and encourages stakeholder participation in policy assessments and advocacy. The findings highlighted the potential for enhancing the access to affordable CVD drugs not only in Sri Lanka, but also adaptable to other LMICs. These outcomes can contribute to policy decisions, aimed at reducing the significant global burden of CVD.

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1. Introduction

Cardiovascular diseases (CVD) stand as the leading cause of global fatalities, accounting for approximately 28% of all deaths.[1-3] The World Health Organization (WHO) states that CVD affects all countries regardless of geographic, socioeconomic, or gender boundaries. Low and middle-income (LMIC) countries contribute to about 80% of CVD deaths, making it a significant public health challenge.[4,5] The burden of CVD remains disproportionately higher in LMICs compared to high-income countries (HICs). The economic loss due to CVD in LMICs amounted to 3.7 trillion USD between 2011 and 2015, representing approximately half of the non-communicable disease economic burden and 2% of the gross domestic product across LMICs.[6]

Despite the elevated political commitment to improve CVD outcomes by 2025,[7] most countries are off course to meet the targets.[6] In many LMICs, particularly in the poorest settings, even meeting all the globally adopted risk factor targets may not be sufficient to achieve the global target of a 25% reduction in CVD mortality by 2025.[8] The challenges of health systems in LMICs, such as insufficient health spending, poor governance, inefficient care delivery systems and focus on curative care at the expense of prevention, have been suggested to contribute more to the CVD burden than individual risk factors, which remain low in LMICs.[9] Crucially, secondary prevention medicines for CVD remain unavailable and unaffordable in many LMICs.[10,11]

Sri Lanka has a population of 21.7 million people and is in the late stages of demographic and epidemiological transition. The state sector remains the key provider of inpatient care,[12,13] with a rate of 4 beds per 1000 population.[14] Government spending as a share of gross domestic product for health has remained less than 2% for many years.[13] Sri Lanka's health system faces challenges from an ageing population and the burden of non-communicable diseases, which currently contribute to nearly 75% of deaths in the country. The majority of services in the country, including inpatient (95%) and outpatient care (50%) are provided by the public sector.[13] Curative care encompasses different levels, from outpatient-only facilities and primary care institutions to tertiary-care institutions and specialised hospitals. The state provides patients with a comprehensive range of health care services and medicines, free of charge.[10,15]

Implementation research plays a crucial role in reducing research waste by identifying approaches that facilitate the translation of research findings into application.[16] The successful implementation of health system interventions depends on various factors, such as organisational context, the strategies employed, and the perceptions of those delivering and receiving the intervention.[17] While promising health interventions may show effectiveness in pilot studies, their real impact on populations can only be realised when they are deployed at scale across communities and healthcare systems. Scaling up of effective health interventions is essential to ensure that communities have access to the most beneficial services and programs. To aid policymakers and practitioners in systematically assessing the feasibility of scaling up health interventions, the Intervention Scalability Assessment Tool (ISAT) was developed.[18]

The objectives of this study were twofold: to systematically review existing literature on interventions for the cost containment of drugs used for CVDs; and then explore the adaptability of identified interventions to Sri Lanka by using the ISAT, with participation from Sri Lankan healthcare stakeholders. In addition to assisting the broader endeavour of promoting greater global health equity in respect to CVD burden, this study aimed to support evidence-based decision-making for methodical assessments of the suitability of interventions for scale-up to different LMIC settings.

2. Materials and methods

2.1. Component one

The publications included in the literature review were selected based on the inclusion criteria (Table 1), categorised using the Population, Intervention, Comparison and Outcome (PICO) framework.

The review followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) strategy (Fig. 1), which allows a systematic selection of articles. The protocol was registered in the international database of prospectively registered systematic reviews in health and social care, Centre for Reviews and Dissemination, University of York (No: CRD42022367957).

The PICO framework for this review was established as follows: the population of interest was individuals with CVDs who need drug treatment. The interventions considered are health system interventions observing cost containment of cardiovascular drugs. This is compared either over time, between different regions, or between groups that employ usual practice or no intervention. The outcome examined was drug cost containment, which can be measured in terms of drug expenditure, cost-effectiveness, or access to drugs. A comprehensive literature search was undertaken using multiple databases: Medline, Embase and Web of Science. The search was conducted using the following terms:

- The pharmaceutical terms (#1): The search included keywords such as "drug*", "medicament*", "medication*", "medicine*", "pharmaceutical*", and "prescription*" in the AB (abstract) or TI (title) fields, along with the MeSH term "Pharmaceutical preparation*."
- Cardiovascular terms (#2): The search terms such as "cardiovascular*", "cardiac*", "coronary*", "heart*", and "myocardial*" in AB or TI, supplemented by the MeSH term "cardiovascular system*.
- Cost related terms (#3): The search also included keywords such as "cost* reduc*", "cost* contain*", "cost* sav*", "price* reduc*", "price* contain*", "price* sav*", "expen* reduc*", "expen* sav*", and "expen* contain*" in AB or TI, along with the MeSH term "cost control*."

Table 1
Inclusion and exclusion criteria according to PICO and study design.

Item	Inclusion criteria	Exclusion criteria
Population	Individuals with CVDs who require drug treatment	-
Intervention	Health system interventions aimed at cost containment of drugs used for CVDs	Interventions aimed at cost containment of drugs other than used for CVDs
Comparator	Comparison over time, between regions or between groups of the usual practice or no intervention	-
Outcome	Measure of drug cost containment, such as drug expenditures, cost effectiveness, or access to drugs	-
Study design	Studies reporting original research with any study designs; Peer reviewed publications after year 2010	Non-original research, and commentary and opinion pieces; Publications done in other languages Letters, editorials, unpublished grey literature, guidelines, conference proceedings, case reports, methodology papers and literature reviews

PICO: Population, Intervention, Comparison and Outcome; CVDs: cardiovascular diseases; -: not applicable.

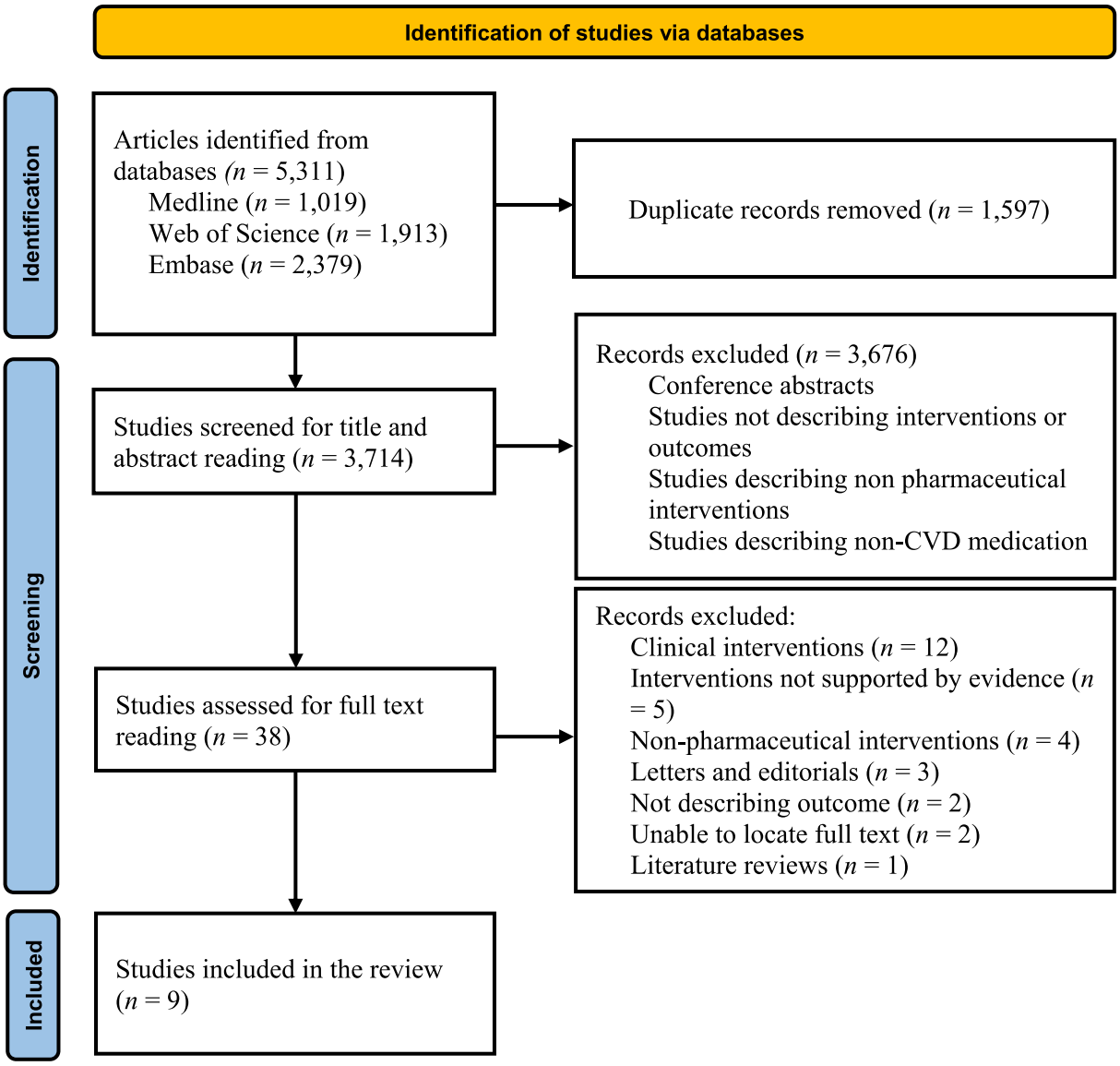

Fig. 1. Preferred Reporting Items for Systematic Review and Meta Analysis (PRISMA) strategy.
CVDs: cardiovascular diseases.

- The terms from each category were combined using the Boolean operator AND (#1 AND #2 AND #3) to refine and narrow the search results.

The initial search was conducted in August 2023. Before the submission, we reran the search in December, 2023, to ensure the inclusion of any recent articles. This subsequent search did not yield any additional articles.

The search strategy was aimed at capturing all interventions published after 2010 that focused on the cost containment of drugs used for the treatment of CVDs. Inclusion was limited to articles written in English language. Letters, editorials, unpublished grey literature, guidelines, conference proceedings, case reports, methodology papers and literature reviews were excluded. Data were extracted from the selected articles using summary tables, then thematically synthesised.

A rigorous verification procedure was practised to assure the accuracy of the data summaries and synthesis. Each article's extracted material was rigorously cross-referenced with the original sources to validate and correct any potential mistakes or omissions. The summaries were thoroughly reviewed and discussed with the study team, with the goal of ensuring consistency. During this review process, any differences or doubts were resolved through collaborative consensus-based discussions.

Risk of bias was analysed using the Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I). The risk of bias was graded into low, inconclusive, or high, as described below: Low: Low or Moderate (ROBINS-I) risk of bias rating; Inconclusive: Serious (ROBINS-I) risk of bias rating; High: Critical or no information (ROBINS-I) risk of bias rating.

2.2. Component two

The health system interventions reviewed in this study were categorised by the research group, considering inputs from health economists, health system researchers, and health managers. From the included articles in the final review, intervention themes were extracted by careful assessment. For the adaptation of these themes to Sri Lanka, the research team employed the ISAT.[18]

The ISAT is a decision support tool designed to assist policy makers and implementers in assessing the sustainability of health interventions for scale up. This tool consists of two parts, each composed of five do-

Table 2
Characteristics of the interventions for the cost containment of CVD drugs ($n = 9$).

Characteristic	Studies [n (%)]
Year of publications	
2010–2015[19-22]	4 (44.4)
2016–2020[23-25]	3 (33.3)
After 2021[26,27]	2 (22.2)
Study country	
Asia[23,25,26]	3 (33.3)
Europe[20-22,24,27]	5 (55.5)
Oceania[19]	1 (11.1)
Economic level of the countries	
High-income countries[19-22,24,26,27]	7 (77.8)
Other[23,25]	2 (22.2)
Scale of the intervention	
National level[20,21,23,25,27]	5 (55.6)
Regional level[19,22,24,26]	4 (44.4)

CVD: cardiovascular disease.

mains. Domains of part A includes A1: Problem, A2: Intervention, A3: Strategic/Political context, A4: Evidence of effectiveness and A5: Intervention cost and benefits. Domains of part B includes B1: Fidelity and adaptation, B2: Reach and acceptability, B3: Delivery setting and workforce, B4: Implementation infrastructure and B5: Sustainability. Part A includes six questions, while part B includes 12 questions. Each question has four levels, zero signifying 'not applicable/not at all', one denoting 'agree to a small extent', two indicating 'agree somewhat', and three meaning 'agree to a large extent'. The possible range of scores can vary from zero to three for any responses. Based on the responses to these questions by the study participants, an average score was given separately to each question for all six intervention themes. After calculating the average response values of the participants in conjunction with ISAT, separate radar plots were generated and mapped.

The selection and adaptation of the ISAT to the Sri Lankan health system was executed by Sri Lankan healthcare stakeholders, which included purposively selected health managers ($n = 5$), cardiologists ($n = 5$), pharmacists ($n = 5$), nursing officers ($n = 5$), and cardiac patients ($n = 5$). All stakeholders, apart from the patients, had worked in the Sri Lankan health system for more than five years. Data were collected from each individual participant ($n = 25$) through independently conducted interviews. Prior to data collection, the articles selected from the component one and their summaries were distributed among the participants, providing them with an opportunity to inquire about any areas requiring clarification.

Ethical approval was obtained from the Postgraduate Institute of Medicine (PGIM), (ERC/PGIM/2022/193) prior to the commencement of data collection. Information sheets and consent forms were distributed and explained before any data was gathered. Participation in this study was completely voluntary.

3. Results

Results of the systematic review (component one) and adaptation of the selected intervention themes to Sri Lanka (component two) described separately.

3.1. Component one

A total of 5,311 articles were initially identified. After removing duplicates, there were 3,714 articles for title and abstract review. We then excluded 3,676 articles that did not meet the inclusion criteria after title and abstract screening. After assessing 38 articles through full-text screening, nine articles were included (Fig. 1).

Table 2 shows that the majority of studies ($n = 4$, 44.4%) were published between 2010 and 2015, with smaller proportions published between 2016–2020 ($n = 3$, 33.3%) and 2020–2022 ($n = 2$, 22.2%). The studies were conducted in a variety of countries, including India and China in Asia, Portugal, Spain, Germany, Austria, the Netherlands, Norway, and Slovakia in Europe, and Australia in Oceania. Seven studies were conducted in high-income countries, with most ($n = 5$) undertaken in Europe. Approximately 55.6% ($n = 5$) of the studies were implemented at the national level, while the remaining were conducted at the regional level. Almost all the interventions were successful at the trial level, but there were recorded instances of the failure at health system level.

The manuscript summaries, including author names, descriptions and outcomes are presented in Table 3.

3.2. Component two

Six intervention themes were identified from the nine studies included in the review are listed below and these themes were considered by key informants for adaptation to Sri Lanka using ISAT: (1) imposing a ceiling price/reference price;[20,21,23,25] (2) introduction of a polypill;[19] (3) introducing volume price contract initiatives;[26] (4) regulating the prescribing of generics and essential drugs[20,24,27]; (5) intervention package 1 which includes generics, essential medicines, 90-day drugs (given drugs for 90 days), and free delivery[27]; and (6) Intervention package 2 which includes discounts, rebates, cost-free medicines, Bundling.[22]

Six intervention themes were considered for assessing the feasibility of adaptation to Sri Lanka. Intervention theme one, "Imposing ceiling price/reference price," was supported by four manuscripts.[20,21,23,25] Intervention theme four, "Regulating the prescribing of generics and essential drugs," was related to three manuscripts,[20,24,27] while the other four intervention themes were each supported by one paper.[19,22,26,27] The Fig. 2 displays separate radar plots for six intervention themes.

For intervention theme one (Imposing ceiling price/reference price), among the A domains A2 (intervention) had the highest score (2.64) indicating that overall, respondents 'agreed to a large extent' with the 'Description of the proposed program/intervention to address the problem', while A1 (problem) had the lowest rating (2.08), indicating that overall, respondents 'agreed somewhat' that there was 'Consideration of the problem that is being addressed'. Notably, all A domains had scores higher than 2, demonstrating their applicability to the Sri Lankan context. B3 (delivery setting and workforce) obtained the lowest score (1.91), indicating respondents 'agreed to small to somewhat extent' that there was 'Consideration of the setting within which the intervention is delivered as well as the delivery workforce' among the B domains, whereas the remaining four B domains received scores above 2, indicating respondents agreed 'somewhat' or 'to a large extent', that there was acceptable consideration of the fidelity and adaption of intervention (B1), reach and acceptability (B2), consideration of the implementation infrastructure (B4) and consideration of longer-term outcomes and sustainability (B5).

For intervention theme two (introduction of a polypill), all five A domains (Problem, intervention, strategic/political context, evidence of effectiveness and intervention cost benefits) scored higher than 2 indicating respondents agreed 'somewhat' or to 'a large extent'. The B domains (fidelity and adaptation, reach and acceptability, delivery setting and workforce, implementation infrastructure and sustainability), on the other hand, received scores below 1.5 indicating 'agree to a small extent' or 'somewhat', with B3 (delivery setting and workforce) recording the lowest score (1.09) indicating 'agree to a small extent' that there was 'Consideration of the setting within which the intervention is delivered as well as the delivery workforce'.

Intervention theme three (introducing volume price contract initiatives); A1 (problem) indicated the best score (2.48), indicating respondents agreed 'somewhat' or 'to a large extent' with the highest score among all domains, and all A domains (problem, intervention, strategic/political context, evidence of effectiveness and intervention cost benefit) exceeded the 2-point criterion indicating respondents agreed

Table 3
Summary of manuscripts.

Author & Year	Description	Outcome	Quality assessment
Atal et al., 2016[23]	The research examines the impact of India's Drug Price Control Order (DPCO) on the prices of commonly used drugs, aiming to provide consumers with affordable access to essential drugs. By comparing the prices of 50 price-controlled pharmaceuticals against non-price-controlled branded drugs, the study reveals significant cost differences, attributed to reduced production and marketing expenses resulting from DPCO constraints, including limited manufacturer profit margins and marketing techniques. Additionally, the study highlights considerable price variation among price-controlled pharmaceuticals, underscoring the necessity for enhanced implementation of price control measures	The study indicates that price control has effectively reduced drug prices, but there is room for improvement in policy implementation. Ongoing efforts are necessary to strengthen the efficiency of price control mechanisms and provide affordable access to vital drugs for patients	Low risk of bias
Gama et al., 2017[24]	This focuses on the promotion of generic and essential drugs in Portugal for CVD. It investigates the advantages of taking CVD drugs in terms of cost savings, greater access to drugs, and efficacy. The study examines physicians' prescription practises, focusing on the usage of generic and essential drugs. It reveals significant diversity among physicians in prescribing, with some prescribing more frequently than others. The study also reveals that using generic and essential medicines can result in significant cost savings that can be used to fund other healthcare initiatives. The study claims that these medicines are as effective as branded alternatives but far less expensive, making them a more cost-effective option for both healthcare providers and patients	Encouraging the use of generics and essential drugs can result in significant cost savings, greater access to drugs, and successful management of CVDs. The study emphasises the ongoing need to educate healthcare providers and patients about the benefits of these medications and to address any barriers to their use	Low risk of bias
Khanijo et al., 2020[25]	The article investigates how drug price controls affect the CVD drug cost in India. It investigates the pricing of these drugs before and after the DPCO, a regulatory structure aimed at assuring affordable access to vital drugs. The study compares the prices of essential to non-essential CVD drugs that are not subject to price control under the DPCO. It also investigates the relationship between the level of essentiality and drug prices, attempting to determine whether more essential drugs are priced lower than non-essential drugs. The findings show that CVD drugs are significantly less expensive than non-essential drugs that are not subject to price control. Moreover, drugs considered more important are priced lower than those considered less vital. The study emphasises the importance of effective price control policies in reducing the cost of essential drugs and underscores the ongoing need to improve the availability and affordability	This study highlights understanding of the influence of drug pricing regulations on the cost of CVD drugs. The findings demonstrate that price control policies effectively promote affordable access to essential drugs, ultimately improving patient outcomes in CVD care. These data emphasise the importance of prioritising essential drugs for CVDs because they provide significant health benefits at a lower cost than non-essential drugs	Low risk of bias
Laba et al., 2014[19]	The article investigates the financial benefits of utilising a polypill, which is a mixture of drugs, to treat CVD in Australia. It examines the outcomes of the Kanyini GAP study, which assessed the polypill's efficacy and cost-efficiency in managing CVDs. The cost of the polypill is compared to the cost of individual medications commonly used for CVD prevention and treatment. The study showed that utilising a polypill is cost-effective in compared to individual drugs for CVD management in Australia. It expects that the polypill will result in significant cost savings, owing mostly to decreased pharmaceutical costs and increased adherence to treatment regimens. The study shows the potential benefits of using a polypill, such as increased drug availability and health outcomes	The data imply that the polypill can lead to large cost savings and better health outcomes, making it a cost-effective choice for CVDs. This emphasises the importance of ongoing efforts to promote polypills and ensure their effective and efficient implementation. It stresses the continuous need to encouraging use of polypills in different nations coping with CVDs as a serious health concern	Low risk of bias
Li et al., 2021[26]	The study looks at how volume-price contracts (VPCs) affect drug pricing at public hospitals in China's Hubei Province. VPCs provide drug price savings to hospitals that purchase larger volumes of pharmaceuticals. The study compares drug prices purchased through VPCs to those purchased outside of VPCs. The findings show that the use of VPCs is associated with lower drug prices in those public hospitals. The study focusses the potential benefits of using VPCs to reduce drug pricing in public hospitals. This emphasises the importance of continuously monitoring VPC and ensuring their effective implementation. According to the report, regulators in China should explore implementing VPCs as part of a holistic approach to regulate medicine prices and increase CVD drug availability	The data indicate that VPCs can successfully cut prescription prices and enhance patient access to cheaper drugs. Furthermore, they have been shown to be more effective in lowering the prices of drugs with larger market shares and higher initial prices. It highlights the significance of ongoing efforts to promote and effectively use VPCs in different healthcare settings	Low risk of bias

(*continued on next page*)

Table 3 (*continued*)

Author & Year	Description	Outcome	Quality assessment
McIntyre et al., 2021[27]	To address CVD drug cost issues, the authors offer different ways include increasing public drug coverage to include all Canadians, instituting a catastrophic drug insurance programme to protect consumers from high out-of-pocket expenditures, and revising prescription pricing and payment processes to assure inexpensive drugs. The article also highlights the ability of generic drugs and therapeutic alternatives to reduce prescription expenditures	This advocates for ongoing efforts to improve access to cheap drugs and emphasises the need of teamwork and stakeholder participation in addressing this vital public health issue. It emphasises the need of patient education and participation in promoting drug adherence and achieving optimal health outcomes	Inconclusive risk of bias
Plans-Rubio, 2010[20]	The article focuses on the cost-effectiveness of statin therapy in Spain, particularly following the advent of generic drugs and the imposing of reference pricing laws. While statin therapies are effective in reducing CVD risk, their high-cost poses challenges for healthcare systems and patients. The introduction of generics and reference pricing in Spain aims to lower medication costs and enhance access. Through a cost-effectiveness analysis, the author investigates the costs and benefits of statin therapy before and after the introduction of such regulations	The study provides valuable insights into the impact of pharmaceutical policies on drug costs, underscoring the need for continuous research and analysis in this field. The analysis reveals a significant reduction in the cost of statin therapies following the introduction of generics and reference pricing	Inconclusive risk of bias
Vogler et al., 2013[22]	This explores pharmaceutical company discounts and rebates for hospital drugs in five European countries: Austria, Germany, Poland, Portugal, and the United Kingdom. The study sought to identify and compare the types and extent of hospital medicine discounts and rebates, as well as the criteria used to establish them. Authors employed a similar framework to analyse the various discount and rebate systems across nations, with an emphasis on price transparency, percentage of reductions granted, timing and frequency of discounts, and eligibility restrictions. Data were gathered from publicly accessible sources such as government websites and reports, as well as pharmaceutical publications. They noted that the differences in pricing structures may be due to the variation in the healthcare systems and market structures across the countries and discovered that the timing and frequency of discounts and refunds varied greatly, with some nations providing yearly discounts and others providing per-unit reductions	The study emphasises the importance of collaboration and sharing best practises among countries, as well as the need for greater transparency and consistency in the pricing of hospital medicines across Europe. According to the authors, greater collaboration may result in more favourable pricing arrangements, as well as increased efficiency and cost savings for healthcare systems	Inconclusive risk of bias
Stargardt, 2010[21]	The study investigates the impact of reference pricing on patients' switching behaviour and healthcare utilization in the German statin market. Reference pricing restricts reimbursement to a set level, necessitating patients to cover the difference for more expensive prescriptions. Using claims data from a large German health insurance from 2001 to 2004, the research examines statin users' behaviour before and after reference pricing introduction	Reference pricing effectively lowers drug prices through increased price competition. However, there were no significant changes in healthcare utilization patterns for statin users after reference pricing implementation	Low risk of bias

DPCO: Drug Price Control Order; CVD: cardiovascular disease; VPCs: volume-price contracts.

'somewhat' to 'a large extent'. The B domains (fidelity and adaptation, reach and acceptability, delivery setting and workforce, implementation infrastructure and sustainability), on the other hand, had scores less than 2, indicating 'agree to a small extent' with B2 (reach and acceptability) indicated the highest (1.94) indicating close to 'agree somewhat' that there was 'Consideration of the reach and acceptability of the intervention for the target population'.

Intervention theme four (regulating the prescribing of generics and essential drugs); both domain A (problem, intervention, strategic/political context, evidence of effectiveness and intervention cost benefit) and domain B (fidelity and adaptation, reach and acceptability, delivery setting and workforce, implementation infrastructure and sustainability) had ratings more than 2, indicating their acceptance 'agree somewhat' to 'a large extent'. Domain A1 (problem) received the highest score (2.73) close to maximum or 'agree to a large extent' that there was 'Consideration of the problem that is being addressed', while domain A4 (implementation infrastructure) received the lowest (2.02) indicating 'agree to somewhat' that there was 'Consideration of the level of evidence available to support the scale-up of the proposed intervention'.

Intervention theme five (intervention package one including generics, essential medicines, 90-day drugs, and free delivery); Among the A domains, A1 (problem) obtained the greatest score (2.31) indicating 'somewhat' or 'to a large extent' that there was 'Consideration of the problem that is being addressed', while A4 (Evidence of effectiveness) received the lowest (2) indicating 'agree somewhat' that there was 'Consideration of the level of evidence available to support the scale-up of the proposed intervention'. All A (problem, intervention, strategic/political context, evidence of effectiveness and intervention cost benefit) domains had an average score of 2 or above indicating 'agree somewhat' to 'a large extent'. B2 (reach and acceptability) had the highest score (1.94) in the B domains indicating close to 'agree somewhat' that there was 'Consideration of the reach and acceptability of the intervention for the target population', while B3 (delivery setting and workforce) received the lowest score (1.39) indicating 'agree to a small extent' that there was 'Consideration of the setting within which the intervention is delivered as well as the delivery workforce'. None of the B domain exceeded the score more than 1.5 level except B2 (reach and acceptability) indicating the absence of respondents 'agree to a large extent'.

Intervention theme six (intervention package two including discounts, rebates, cost-free medicines, bundling); A1, A2, and A5 (problem, intervention, and cost and benefits) earned scores greater than 2 indicating 'agree somewhat' to 'agree to a large extent', while A3 and A4 (strategic/political context and evidence of effectiveness) obtained scores less than 1.5 indicating closer response for 'agree to a small extent'. B3 (delivery setting and workforce) received the lowest score (1.11) of the B domains indicating 'agree to a small extent', while B4

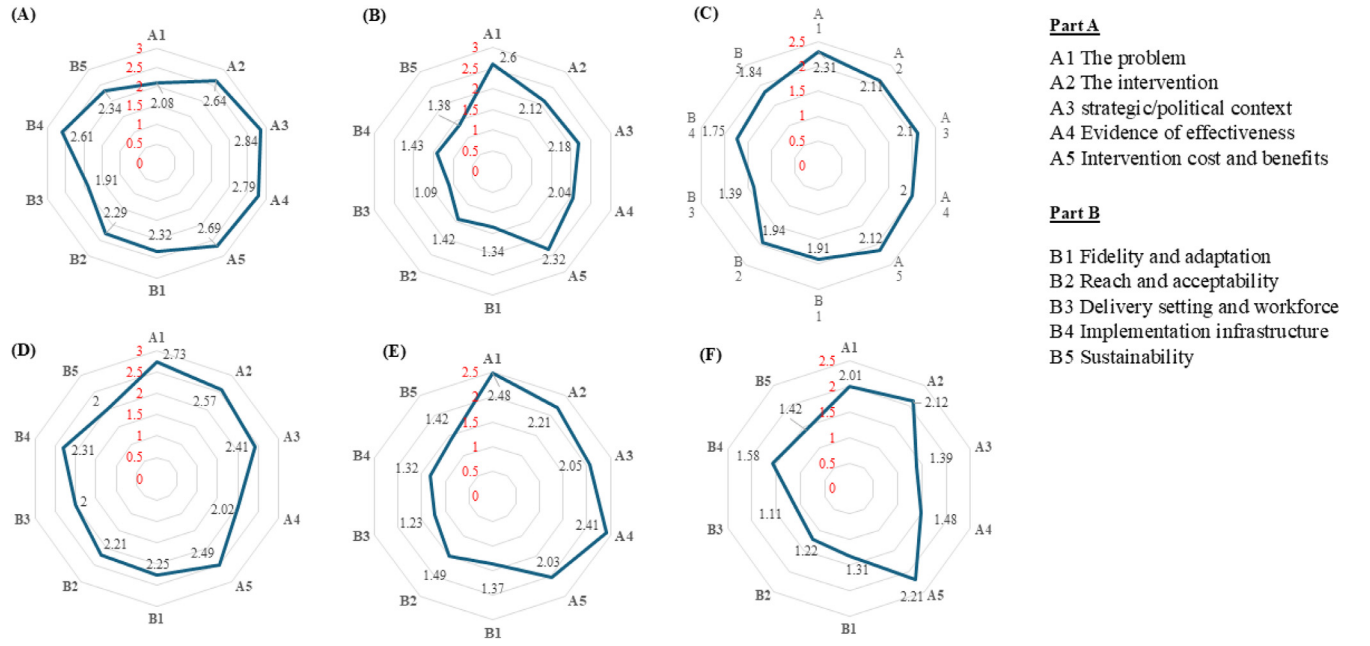

Fig. 2. Results of the Intervention Scalability Assessment Tool (ISAT) radar plots for six intervention themes. (A) Theme one (ceiling/reference price); (B) Theme two (polypill); (C) Theme three (volume price contact); (D) Theme four (generics and essentials); (E) Theme five (package one); (F) Theme six (package two).

(implementation infrastructure) had the greatest score (1.58) indicating closure value to 'agree somewhat'. Except for B4, all B domain scores were less than 1.5 indicating 'agree to a small extent'.

4. Discussion

The present study explored the perceptions of selected stakeholders in Sri Lanka, by employing ISAT framework to recognize the acceptable and applicable interventions for CVD drug cost containment, for the Sri Lankan context. Selected stakeholders perceived that, interventions related to ceiling or reference price (Fig. 2) and generic and essential prescribing (Fig. 2) were the most favourable ones, and other interventions (Fig. 2) were rated poorly. However, there were perceptual variations between different stakeholder groups, which highlighted the need for addressing these variations with stakeholder engagement prior to the implementation of these selected interventions in Sri Lanka.

The ISAT is commonly regarded as an instrument for assessing the potential scalability of health interventions and showing their effectiveness in real-world scenarios.[28] It provides a systematic approach for assessing the scalability of population-level health interventions, identifying evidence-based strengths and weaknesses for scale-up, and flagging possible scale-up implementation issues.[29] The ten domains of ISAT have a series of questions targeted at checking preparedness for scale-up of interventions and assisting in identifying strengths and weaknesses in the evidence.[29,30] Scaling-up healthcare innovations are important in the contemporary world because it minimizes waste and inequities in health and social settings while spreading the benefits of effective and evidence-based innovations.[31]

All six selected intervention themes had a favourable influence on health system development in their original contexts, but the predicted outcomes in Sri Lanka as perceived by the study participants were not uniform. Although many components of the interventions had the potential for scale-up, as indicated by high scores (2–3), there were concerns about other domains, notably for those which are linked to delivery setting and workforce, and sustainability (B3 and B5), which obtained comparatively lower values (1–2). However, the idea of scalability is always evolving, necessitating regular updates of tool-based interventions.[18]

Scaling up successful health interventions is critical for achieving population-wide benefits.[32,33] Cost containment of CVD drugs is important to improve access to CVD drugs, and thus contribute to medication adherence and improved clinical and population-related outcomes for CVD patients.[34] The imposing of the ceiling or reference price (theme one) obtained the highest score of all the interventions. In contrast, intervention package two (theme six) was the least prioritised intervention theme among Sri Lankan participants. However, there were variations of perceptions among different stakeholders and according to the research, stakeholders should collaborate closely with key groups to gain critical support for health system interventions, conduct rigorous evaluation research to determine the effects of system interventions, and, where possible, reduce the administrative burden.[35]

Imposing a ceiling price or reference price and controlling the prescribing of generics and essential drugs (Fig. 2), were perceived as the most acceptable by the Sri Lankan participants. Furthermore, stakeholders reported a strong need for price control and a readiness to pay less for generics of important CVD drugs, which is a shared concern of other LMICs.[36] The study's findings underline the importance of focusing attention on making drugs used in chronic illnesses more financially accessible, particularly in the public sector.[37]

The introduction of a polypill, the implementation of volume price contract initiatives, intervention packages one and two (Fig. 2) were all scored poorly by Sri Lankan participants, but none of the intervention themes scored less than one for any sub domains. Nevertheless, integrating medication adherence interventions into routine care remains a challenging endeavour.[38]

Given the importance of intervention scalability and measurement, important factors should be examined during the planning, design, and implementation of interventions.[39] It allows academics, policymakers, and practitioners to use prior scale-up experiences to model future scaling-up of health interventions. Given the significant variance in scaling up of interventions across contexts and routes, documenting critical processes and understanding variations in delivery settings and scale-up contexts provide helpful insights for comparable programmes requiring scaling up.[40,41]

This study aimed to prioritise interventions to address the cost containment of CVD drugs based on impact and acceptability, provide opportunity to modify interventions to the local context, and offer platform

for stakeholder collaboration to improve evaluation of interventions and advocacy for policy and funding support. This study emphasises the significance of strategic intervention selection, adaption to local requirements and contextual considerations with the stakeholder engagement and lobbying for supporting policies and financing.

The present study has a few limitations that need to be acknowledged. Firstly, the sample size of 25 participants for component two is relatively small, which could potentially limit the generalisability of the findings. This small sample might not capture the full range of perspectives across different stakeholder groups in Sri Lanka, and therefore, the representativeness of the results could be affected. Secondly, the interventions included in the systematic review had significant heterogeneity in terms of their implementation contexts, target populations, and healthcare systems. This variability makes it challenging to make direct comparisons and may limit the applicability of certain interventions to the Sri Lankan context. Finally, while the study utilised the ISAT framework to assess the scalability and adaptability of interventions, practical challenges related to actual implementation were not fully explored. Factors such as resource constraints, political will, and infrastructure limitations, which are crucial for successful implementation, were not addressed in detail. These aspects could significantly impact the feasibility and sustainability of the proposed interventions in real-world settings.

5. Conclusions

The rising global prevalence of CVDs has exacerbated the challenge of expensive medications, particularly in Sri Lanka due to its disease burden and economic factors. Past data underscore the need for cost-effective healthcare solutions. Our study utilized ISAT to assess six health intervention themes for their suitability in Sri Lanka. This study revealed that methods like setting ceiling prices and controlling generic and essential drug prescribing (Fig. 2) were popular, while others (Fig. 2) received lower scores. This approach provides a roadmap for future interventions, drawing on past successes. Understanding contextual variables is vital, given the diversity in scaling interventions. Additionally, our study promotes stakeholder engagement, enhancing assessment and policy advocacy. This evidence-based approach empowers decision-makers to customize interventions, addressing healthcare challenges in various settings.

In conclusion, our research emphasises the importance of careful intervention choice, context adaptation, and stakeholder involvement. This may be important for supporting sustainable, fair access to medicines, reducing the cost of CVD medications, and navigating the challenging world of healthcare economics.

Ethics approval and consent to participate

Ethical approval was obtained from the Postgraduate Institute of Medicine (PGIM), (ERC/PGIM/2022/193) prior to the commencement of data collection. Information sheets and consent forms were distributed and explained before any data was gathered. Participation in this study was completely voluntary.

CRediT authorship contribution statement

Jayasekara Liyana Patabendige Chaminda: Conceptualization, Methodology, Validation, Formal Analysis, Investigation, Writing – original draft. **Sanjeewa Kularatna:** Conceptualization, Methodology, Resources, Writing – review & editing, Project Administration. **Dilantha Dharmagunawardene:** Methodology, Investigation, Writing – review & editing. **Reece Hinchcliff:** Methodology, Writing review & editing. **Alexia Rohde:** Methodology, Writing – review & editing. **David Brain:** Methodology, Writing review & editing. **Ruvini Manjula Hettiarachchi:** Methodology, Writing – review & editing. **Sucharitha Rangi Weerasuriya:** Methodology, Investigation, Validation. **Sunil Senarath Yapa:** Methodology, Project Administration. **Sameera Senanayake:** Conceptualization, Methodology, Project Administration, Writing – review & editing, Supervision.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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