

Building the health-economic case for scaling up the WHO-HEARTS hypertension control package in low- and middle-income countries

Andrew E. Moran^{1,2}, Margaret Farrell¹, Danielle Cazabon¹, Swagata Kumar Sahoo¹, Doris Mugrditchian¹, Anirudh Pidugu², Carlos Chivardi³, Magdalena Walbaum, Senait Alemayehu⁵, Wanrudee Isaranuwachai⁶, Chaisiri Ankurawaranon⁷, Sohel R. Choudhury⁸, Sarah J. Pickersgill⁹, David A. Watkins⁹, Muhammad Jami Husain¹⁰, Krishna D. Rao¹¹, Kunihiro Matsushita¹¹, Matti Marklund^{11,12,13}, Brian Hutchinson¹⁴, Rachel Nugent¹⁴, Deliana Kostova¹⁰ and Renu Garg¹

Suggested citation Moran AE, Farrell M, Cazabon D, Sahoo SK, Mugrditchian D, Pidugu A et al. Building the health-economic case for scaling up the WHO-HEARTS hypertension control package in low- and middle-income countries. *Rev Panam Salud Publica*. 2022;46:e140. <https://doi.org/10.26633/RPSP.2022.140>

ABSTRACT

Generally, hypertension control programs are cost-effective, including in low- and middle-income countries, but country governments and civil society are not likely to support hypertension control programs unless value is demonstrated in terms of public health benefits, budget impact, and value-for-investment for the individual country context. The World Health Organization (WHO) and the Pan American Health Organization (PAHO) established a standard, simplified Global HEARTS approach to hypertension control, including preferred anti-hypertensive medicines and blood pressure measurement devices. The objective of this study is to report on health economic studies of HEARTS hypertension control package cost (especially medication costs), cost-effectiveness, and budget impact and describe mathematical models designed to translate hypertension control program data into the optimal approach to hypertension care service delivery and financing, especially in low- and middle-income countries. Early results suggest that HEARTS hypertension control interventions are either cost-saving or cost-effective, that the HEARTS package is affordable at between US\$ 18-44 per person treated per year, and that antihypertensive medicines could be priced low enough to reach a global standard of an average <US\$ 5 per patient per year in the public sector. This health economic evidence will make a compelling case for government ownership and financial support for national scale hypertension control programs.

Keywords

Health services accessibility; cost-benefit analysis; hypertension; cardiovascular diseases.

¹ Resolve to Save Lives, New York, United States of America ✉ Andrew Moran, amoran@resolvetosavelives.org

² Columbia University Irving Medical Center, New York, United States of America

³ Center for Health Economics, University of York, York, United Kingdom

⁴ Care Policy and Evaluation Centre, London School of Economics and Political Science, London, United Kingdom

⁵ Ethiopian Public Health Institute, Addis Ababa, Ethiopia

⁶ Health Intervention and Technology Assessment Program, Ministry of Public Health of Thailand, Bangkok, Thailand

⁷ Department of Family Medicine, Chiang Mai University, Chiang Mai, Thailand

⁸ National Heart Foundation of Bangladesh, Dhaka, Bangladesh

⁹ University of Washington, Seattle, United States of America

¹⁰ Division of Global Health Protection, Centers for Disease Control and Prevention, Atlanta, United States of America

¹¹ Johns Hopkins Bloomberg School of Public Health, Baltimore, United States of America

¹² The George Institute for Global Health, Faculty of Medicine, University of New South Wales, Sydney, Australia

¹³ Department of Public Health and Caring Sciences, Uppsala University, Uppsala, Sweden

¹⁴ Center for Global Noncommunicable Diseases, RTI International, Seattle, United States of America

The World Health Organization (WHO) Global Action Plan for the Prevention and Control of Non-Communicable Diseases (NCDs) 2013-2020 called for a 25% relative reduction in the prevalence of raised blood pressure.(1) Concurrent health economic studies recommended hypertension treatment and control among eight “best buy” interventions that, if implemented broadly, would facilitate reaching global NCD control goals.(2) However, in the interval since 2013, and especially since the onset of the COVID-19 pandemic in 2020, few countries have committed significant resources toward NCD control. Across 48 low- or middle-income countries (LMICs) for which disease-specific funding levels are available, only 26% of total health spending (public sector, private sector, and patient out-of-pocket) was devoted to NCD control in 2019,(3) despite that 54% of deaths were due to NCDs. (4) Similarly, despite evidence that NCDs contribute to about two-thirds of preventable global burden of disease, funding for global NCD control constituted only <2% of total development assistance for health in LMICs in 2020.(5) To reach global NCD control goals and reduce fatal and non-fatal burden of disease, more resources toward NCD control are needed. Country governments in particular face constrained health budgets and need evidence that the health and economic benefits justify an investment in hypertension control programs.

Past health economic analyses generally found that hypertension control programs are cost-effective,(6) with most cost-effectiveness ratios estimated in these studies below the affordability threshold recommended for low- or middle-income country payers (not exceeding the average gross domestic product of LMICs). However, the evidence to date is mostly based on small sample sizes and clinical trials where selection bias may be at play. When medication prices are low, as in the public sector of India (average below \$ 5 per patient per year), hypertension control may in fact overall *save money*, while saving lives, because when antihypertensive medication costs are low enough, avoided cardiovascular disease treatment costs outweigh the cost of treating and controlling hypertension.(7) Despite the strength of the evidence favoring investment in hypertension control programs, individual countries are not likely to allocate budget toward hypertension control without country-context specific estimates of favorable health outcomes and affordable budget impact.

In 2016, WHO introduced the HEARTS technical package as a framework for cardiovascular disease (CVD) prevention at the primary health care level.(8) HEARTS is a set of standardized guidelines for screening and management of CVD risk factors. It outlines approaches for lifestyle modification and pharmaceutical treatment of metabolic risk factors such as hypertension, diabetes, and hyperlipidemia. The set of guidelines is organized around six components: H: Healthy lifestyles counseling; E: Evidence-based treatment protocols; A: Access to essential medicines; R: Risk-based management; T: Team-based care; S: Systems for monitoring. The WHO HEARTS technical package recommends a standard, practical approach to hypertension control including simple, standardized treatment protocols using specific recommended medications and devices, a reliable supply of affordable, good quality medications, team-based and community-based care, and a robust health-information system.

The objective of this study is to report on health economic studies that are describing and quantifying the value of implementing HEARTS in LMICs and support the health and economic value of country and donor investment in hypertension control.

ANTIHYPERTENSIVE MEDICINES MARKET RESEARCH IN LOW- AND MIDDLE-INCOME COUNTRIES

Antihypertensive medication availability in LMICs—registration, essential medicines lists, and treatment guidelines

The “A” in HEARTS is Access to essential antihypertensive medicines. Medicines access is a function of availability and affordability, as well as adequate financing and a well-functioning procurement, inventory, and supply chain management system. The quality-assured antihypertensive medicines recommended in the HEARTS technical package and the 2021 WHO hypertension treatment guidelines have been on the market for years and are produced by many manufacturers. However, this does not guarantee that people with hypertension will have access to essential, quality-assured antihypertensive medications across all countries. Manufacturers tend to focus their products on high-income markets where a larger revenue is anticipated, thus largely excluding LMICs. Several studies have assessed the regulatory factors that facilitate the availability of medicines to patients in LMICs. This includes registration of quality-assured medicines in LMICs, listing of antihypertensive medicines on national essential medicines lists and in national treatment guidelines.

In a study that examined the availability of WHO-recommended antihypertensive medicines, only four countries (7.5%) included all WHO-recommended medicines on their national essential medicines list.(9) When assessing average availability of major antihypertensive medicines from the five main pharmaceutical classes in health care facilities or local pharmacies, generic medicines were found to be more available (61% of surveyed facilities where medicines were available) compared to brand medicines (41% of surveyed facilities), private sector availability was higher than public sector availability (brand medicines and generic medicines had an average availability of 46% and 67% in the private sector and an average availability of 29% and 55% in the public sector, respectively), and availability was higher in high-and-upper-middle income countries than in low-and lower-middle income countries (60% *versus* 54%).

A separate study included single pill combination antihypertensive medicine availability survey in five high-burden LMICs.(10) Single pill combinations are more effective at reducing blood pressure and more convenient for patients, but single pill combination antihypertensive medicines were found to be less available than corresponding single agent pill formulations of the same medicines in these countries, especially in the public sector. Across seven manufacturers surveyed, less than 50% of the selected antihypertensive medicines were registered with both a stringent regulatory authority (United States Food and Drug Authority, European Medicines Authority, or equivalent) and also with the local national regulatory authority in at least one of 18 selected LMICs.

General pricing of HEARTS-recommended antihypertensive medications in LMICs

Prices of HEARTS-recommended essential antihypertensive medicines vary across LMICs. Data from the private sectors of five LMICs gathered in systematic searches of five national regulatory authority databases of Brazil, Lebanon, Nigeria, the Philippines, and South Africa of antihypertensive medicines listed in the 2021 WHO Essential Medicines List revealed higher prices of WHO-recommended antihypertensive medicines than estimated cost-based generic prices for these medicines (prices estimated based on the cost of raw materials, manufacturing, transportation, and a 10% profit margin), suggesting there is room for price decreases.^(10,11) This can be done through price negotiations with manufacturers and initiatives such as pooled procurement mechanisms such as the Pan American Health Organization (PAHO) Strategic Fund, or UNICEF. When prices of medicines included in the PAHO Strategic Fund formulary were compared to estimated cost-based generic prices, two PAHO Strategic Fund medicine prices—for amlodipine 5 mg and hydrochlorothiazide 25 mg (not including added local registration, transportation, and warehousing costs)—were lower than estimated cost-based generic prices, and the price of losartan 50 mg was comparable. Single pill combinations in the PAHO Strategic Fund formulary, however, had a much higher price compared with the cost-based generic price, signaling room for lowering single pill combination prices further through negotiations with manufacturers. A study from 106 developing countries determined that international pooled procurement is particularly effective in lowering medication prices for smaller buyers and those with good capacity for long-term planning.⁽¹²⁾

In India, where many manufacturers of antihypertensive medicines exist, a costing study found that the approximate weighted average cost of medication per patient per year was between \$ 33.9 and \$ 58.4 in the private sector when using single agent pills in the treatment protocols, while in the public sector this was much lower (\$ 2.1–3.9).⁽¹³⁾ Because India has a large market demand for antihypertensive drugs and is also home to the world's largest generic pharmaceuticals manufacturing industry, these average annual prices per patient treated may be considered a benchmark for the lowest in the world currently.

Single pill antihypertensive medication combination pricing in LMICs

Several studies have examined prices of single pill combinations in comparison to their component single agent pill equivalents. In select LMIC private markets, some single pill combinations were found to be less expensive than the combined price of their component single agent pills sold separately.⁽¹⁴⁾ However, these studies also found examples of many single pill combinations that were priced higher than their equivalent single agent pills. When calculating the annual cost of simple treatment protocols in India using private and public sector prices, prices of protocols using single pill combinations were higher than when using single agent pills (e.g. \$ 33.88 to \$ 58.44 in the private sector for protocols using single agent pills compared to \$ 51.57 to \$ 68.83 for protocols using single pill

combinations and in the public sector \$ 2.05 to \$ 3.89 for protocols using separate agent pills and \$ 2.94–\$ 3.98 for protocols using single pill combinations.⁽¹³⁾ When WHO-recommended treatment protocols⁽¹⁵⁾ in other LMICs were costed out, the average per-patient cost of single pill combination-based protocols was often equivalent to single agent pill-based protocols. However, in certain countries, using the lowest single agent pill prices available in the public sector resulted in the lowest cost per patient protocol.

MEASURING THE COST OF HYPERTENSION CONTROL PROGRAMS: THE HEARTS COSTING TOOL

Country support for HEARTS hypertension control program scale up to the national level are conditional on governments understanding the added costs of administering the program and running it at the facility level. A tailored approach for assessing and anticipating HEARTS program costs is offered by the HEARTS costing tool.⁽¹⁶⁾ The HEARTS costing tool is an Excel-based tool for estimating the annual incremental cost of conducting HEARTS activities in the catchment area of participating facilities. It is being employed in a number of countries, where it aims to inform scenarios for program expansion or other programmatic aspects. The HEARTS costing tool has supported cost evaluations of hypertension control programs in several countries.

In 2021, the Mexican states of Chiapas and Yucatan launched the HEARTS program in 20 primary care facilities.⁽¹⁷⁾ A cost analysis of the program in Chiapas found that the types of hypertension medications recommended by the HEARTS program (chlorthalidone, amlodipine, lisinopril) were less costly than those currently in use (telmisartan, hydrochlorothiazide, captopril, enalapril, amlodipine, losartan). In Chiapas, adoption of standardized treatment protocols was estimated to result in a 9.7% reduction in annual medication expenditures relative to maintaining status-quo treatment approaches. In Yucatán, the cost of the HEARTS treatment was slightly higher than current implementation, in part because HEARTS hypertension treatment regimens were more intensive (higher medication dose per regimen step) than status quo regimens. The cost analysis indicated that in both states, shifting some HEARTS program tasks from physicians to nurses and other providers would lead to program savings of \$28,000 in Chiapas and \$197,000 in Yucatan. These potential cost savings represent an opportunity for sustainable scaling up of the HEARTS program across other facilities in Mexico.

In 2018, the Sylhet district in Bangladesh introduced elements of the HEARTS program in four subdistrict facilities. Using costs from each of the representative facilities, local experts conducted a cost analysis to project the cost of expanding the program to the entire population of the four participating subdistricts under two scenarios: a hypertension management program and an integrated risk-based hypertension, diabetes, and cholesterol management program. The study entailed disaggregated cost assessments by function and HEARTS elements, identifying areas for efficiency improvements, such as task-sharing and integrated risk management. The cost of delivering the HEARTS hypertension control program was estimated at \$18 per person treated, with the largest proportion of

costs incurred for antihypertensive medicines (43% of costs), followed by provider time to administer treatment (38% of costs).⁽¹⁸⁾ The analysis found evidence of significant staffing constraints that may limit the scalability of the program. Extensive task shifting between providers would represent a necessary path toward a sustainable future for hypertension treatment in Bangladesh.

In 2020, Ethiopia launched a hypertension control initiative modeled on HEARTS in 58 health centers and 10 primary hospitals across seven regions. Activities included introducing a standardized simple treatment protocol for hypertension along with monitoring of supplies, procurement of validated blood pressure measuring devices, health worker training in screening and treatment protocols, and patient monitoring. So far, relevant cost data has been collected from health centers in the cities of Addis Ababa and Dire Dawa, as well as from representative hospital facilities in the regions of Oromia, Sidama, and Amhara. Collecting information on the cost of program activities in participating facilities enhances understanding of cost drivers, aids in budgeting activities and planning for scale-ups, and allows health officials to coordinate future program resources.

In 2016, Chile initiated a project aiming at standardization of treatment of arterial hypertension to improve the control rate of persons with high blood pressure. The strategy was implemented in one primary healthcare center from Santiago, using two other centers as control groups. A prospective cohort study over a period of 3 years was applied to assess changes in blood pressure control, as well as secondary outcomes including adherence to treatment, medications delivered, therapeutic inertia, and incidence of myocardial infarction and stroke. A cost-effectiveness study is being conducted based on the results from the cohort study, aiming to estimate the costs per mmHg reduction in systolic and/or diastolic blood pressure and the cost-effectiveness of the implementation of the HEARTS strategy in Chile compared to the conventional treatment from the perspective of the Chilean public healthcare system.

In 2022, Philippines launched the Healthy Hearts demonstration project for delivering hypertension services in West Visayas Region, Iloilo Province. This project considers two scenarios for delivering hypertension services in remote areas—a traditional approach utilizing staff and medication resources from the local government, and a hybrid approach incorporating private pharmacy services. Expenditure on medications and basic screening services provided by traditional public health units will be compared to those provided by private pharmacy providers. This comparison will examine the potential relative efficiencies of public-private cooperation in the area of hypertension service delivery.

In 2021, Chiang Mai University applied the HEARTS technical package across 140 health stations in Lampang Province, Thailand. Plans are underway to document costs of activities such as implementing simple standardized treatment protocols, nurse-led care, and telemedicine. Initial consideration has suggested that the simple treatment protocols may be potentially more costly than the standard treatment, but an ongoing cost evaluation will examine in greater detail the implications of harmonizing treatment practices along with shifting service delivery activities on to nurses.

NATIONAL BUDGET IMPACT AND BUSINESS CASE FOR HEARTS HYPERTENSION CONTROL IN LMICS: THE ONLINE HYPERTENSION INVESTMENT CASE TOOL

The Hypertension Investment Case Tool is an online tool designed to estimate the national-level costs and consequences of scaling-up the HEARTS protocol for blood pressure treatment in combination with other hypertension related programs such as sodium reduction policies.⁽¹⁹⁾ Users can set targets for hypertension awareness, treatment, and control rates and for population mean sodium intake to produce estimates of the total budget impact and change in key health and non-health outcomes from their designated program scale-up.

Country-specific default inputs for medication unit costs, salary estimates, and frequency/delivery of care were taken from the HEARTS costing tool but are presented as editable fields in the tool for users to replace with their own data when available. Mark-ups for program-level costs including training, health information systems, governance/administration, health financing, and supply chain strengthening are calculated as an estimated percent of total cost based on WHO estimates⁽²⁰⁾ and are added to the patient-level costs to determine a national budget estimate. Data from STEPS surveys were used to estimate baseline awareness, treatment, and control rates to populate the cascade of care but are also editable by the user. The tool models intervention consequences using a state-transition model that captures the dynamic relationship between disease incidence, prevalence, and mortality. To estimate the impact of reduced population blood pressure on CVD events, we took estimates of the relative risk of new CVD (specific to the degree of blood pressure elevation) from the literature.⁽²¹⁾

Using this state-transition approach the model projects fatal and nonfatal outcomes over time under different implementation scenarios, relative to a status quo or business-as-usual scenario. Projections of prevalent hypertension and CVD cases can be used to estimate the population in need of treatment for the costing exercise, and the differences between scenarios represents the incremental costs. In this way, the model illustrates how greater investment in hypertension/CVD prevention can reduce the population in need of advanced CVD treatment and therefore offset spending on costly CVD services. A new module in the tool that will calculate the financial protection impact of scaling up hypertension control, i.e., averted cases of medical impoverishment or catastrophic expenditure on CVD events. This feature is especially important in the context of the universal health coverage agenda and is a novel extension of the usual NCD investment case approach.

Overall, the Hypertension Control Budget Impact Tool provides a platform for policy makers and health planners to quickly assess the projected impact and cost of scaling up hypertension treatment programs in their country. The model is designed to be maximally flexible and user friendly, allowing for tailored estimates of costs and consequences of, for example, adopting different pharmaceutical regimen protocols, shifting certain tasks from health centers to the community level, or implementing sodium-reduction policies within a country. A future version of the tool will allow the user to do analyses across geographic or socioeconomic groups to better understand the health equity implications of hypertension investment.

ECONOMIC VALUE OF IMPROVING HEARTS HYPERTENSION PROGRAM FINANCING AND IMPLEMENTATION

Several health economic modeling studies are exploring optimal health care financing, medication procurement, staffing and team-based care approaches to support successful HEARTS hypertension programs. In terms of antihypertensive medicines, other studies are exploring the incremental advantages of extended length prescriptions and single pill combination antihypertensive medicines.

Impact of alternative health care financing approaches on HEARTS hypertension control program effectiveness and cost-effectiveness in Bangladesh

Many LMICs like Bangladesh face a high and growing disease burden from NCDs. In 2016, approximately 14 million adults aged ≥ 35 years in Bangladesh had hypertension, although around half had not been diagnosed, nearly 60% not treated, and 82% did not have their blood pressure controlled. (22) Both supply side issues and demand side issues contribute to this suboptimal control rate of hypertension. Financing interventions aimed at the supply side have attracted the interest of policymakers because of their consequent effect on provider behavior, service coverage, and quality of care. (23) Demand side financing interventions that lower financial barriers to access care can have important effects in increasing patient use of health services, and adherence to treatment. An ongoing study aims to model the effects of select supply side (e.g., provider payment mechanisms, line-item budget, capitation, pay-for-performance) and demand (e.g., voucher program that subsidizes cost of treatment for poor patients diagnosed with hypertension) interventions on the following outcomes: proportion of individuals with hypertension who are diagnosed, treated and have their hypertension controlled, and CVD cases and mortality averted. This study will use microsimulation methods to simulate the effect on hypertension management and CVD burden of (i) the alternative provider payment mechanisms and (ii) voucher program and/or conditional cash transfer on patient and population outcomes. (24)

Expanding hypertension treatment capacity by increased workforce, greater task-sharing, and extended prescription duration in India

Another key obstacle for scaling up hypertension management in India and other LMIC is the lack of physicians, who often are the only health workers allowed to treat patients with hypertension. Innovative health system approaches such as delegation of basic tasks to non-physician health workers (task-sharing) has been proposed as a potential strategy to alleviate this problem. In an ongoing study, constrained optimization models are used to estimate the hypertension treatment capacity and salary costs of staff involved in public hypertension care in India and to simulate the potential effects of (1) an increased workforce, (2) greater task-sharing among health workers, and (3) extended prescription periods that reduce treatment visit frequency (e.g., quarterly instead of

monthly). The models include data on hypertension prevalence from national surveys, population size estimates from the World Bank, and information on public healthcare organizations, staff availability, and healthcare salaries derived from published government sources.

In preliminary analyses, it was estimated that only around 8% of ~245 million adults with hypertension can currently be treated by physician-led services in the Indian public health system (assuming the current number of health workers, no greater task-sharing, and monthly visits for prescriptions). Without task-sharing and with continued monthly visits for prescriptions, the least costly workforce expansion to treat 70% of adults with hypertension could require ~1.6 million additional staff (all non-physicians), with ~INR 200 billion (~USD 2.7 billion) in additional annual salary costs. Implementing task-sharing among health workers (without increasing the overall time on hypertension care) or allowing a 3-month prescription period was estimated to allow the current workforce to treat ~25% of patients. Joint implementation of task-sharing and a longer prescription period could treat ~70% of patients with hypertension in India. The findings of the preliminary analyses suggest that the combination of greater task-sharing and extended prescription periods could substantially increase the hypertension treatment capacity in India without any expansion of the current workforce in the public health system. By contrast, workforce expansion alone would require considerable, additional human and financial resources.

Impact of different medication procurement approaches on the coverage of HEARTS hypertension control program health and economic outcomes in India

Globally, the control rate for hypertension is dismal and a massive scale up of population-wide hypertension management is especially important for an LMIC such as India. Regular or uninterrupted supply of medications has been identified as a key facilitator to improve hypertension management at a population level. Healthcare reforms to potentially enable this include implementation of a single treatment protocol with 2-3 classes of antihypertensive medications and an increased use of single pill combination antihypertensive medicines.

In an ongoing study, we estimate the potential economic and operational benefits of medication dispensing reforms to increase hypertension medication treatment coverage in the public health care system in India. Two of the evaluated reforms are (1) focused procurement of the short-list of medications specified by the treatment protocol, and (2) increased utilization of single pill combinations. These reforms are expected to allow a greater medication supply (by volume discount). Although outside the scope of the ongoing study, the increased use of single pill combinations may also improve medication adherence. All reforms will be evaluated individually and in combinations, to be compared to a base case scenario without any of the reforms implemented (i.e., mimicking current practice). The simulation framework will encompass a constrained optimization component to maximize the number of patients to receive adequate medication and a microsimulation component to simulate dispensations to patients. Key input data will be informed by medication utilization patterns from published literature and

medication costs from government sources. The expected outcomes could help inform policy makers in India and other countries who are considering reforms to improve medication procurement and dispensation in the public healthcare.

Evaluating the cost-effectiveness of single pill antihypertensive medicine combination therapy in 24 low- and middle-income countries

Single pill combinations uptake in LMICs remains low, in part due to higher cost and lower availability as described above.^(7,8,25) But, with generic formulations of single pill combinations emerging as the predominant formulations supplied to LMICs, there is potential to scale the use of single pill combinations worldwide, including in resource-limited settings. As countries consider incorporation within national hypertension guidelines, cost-effectiveness evidence is needed on the single pill combinations. The purpose of this analysis is to evaluate the national-level costs and consequences of antihypertensive treatment using single pill combinations. In 24 LMICs spanning all WHO regions (Table 1), the analysis will quantify the expected impact of single pill combinations through two pathways: (1) the impact of overcoming clinical inertia by initiating patients on single pill combinations instead of monotherapy; and (2) the impact of improved medication adherence in patients who replace a pharmacological regimen consisting of two or more single agent pills with a single pill combination regimen.

To analyze how health and economic outcomes differ based on treatment protocol choices, and the use of single pill combinations or single agent pills within them, the study will use an Excel-based probabilistic state-transition model populated with epidemiological data from the IHME Epi Visualizations database (9), WHO STEPS Surveys, and the NCD Risk Factor Collaboration Group (10). The model is further populated with cost data on medication prices and other direct and indirect costs of care (e.g. human resource time, supply chain) from national and international databases, and gray and published literature. Treatment protocols initializing with dual-combination therapy are from WHO HEARTS Evidence-based protocols.⁽¹⁵⁾ The blood-pressure-lowering impact of one-, two-, or three-medication treatment regimens, the effect of single pill combinations on increasing adherence, and translation of blood-pressure lowering to reduction in CVD outcomes are from published literature.^(20, 26, 27)

BARRIERS AND SOLUTIONS TO ADOPTING NATIONAL HEARTS HYPERTENSION CONTROL PROGRAMS

Table 2 lists barriers to implementing national HEARTS hypertension control programs and potential solutions provided by health economic research. The major economic barrier to countries adopting HEARTS hypertension control programs is simply that the budget impact and value for health gain are not well quantified—ongoing costing and health economic evaluations are meant to overcome this barrier. For other barriers to adoption of the full package—e.g., team-based care—despite that the clinical efficacy of team-based care has been studied, more research is needed to describe the detailed economic consequences of team-based care.

CONCLUSIONS

Health economic studies have demonstrated the cost-effectiveness of hypertension control according to standard affordability standards for LMICs; in countries with very low medication costs, hypertension control programs may be cost-saving, whilst saving lives. Country governments and donors require country-context specific investment case for adopting the global standard WHO-HEARTS hypertension control package. Health economic methods are being applied towards describing and quantifying the health and economic impact of implementing WHO-HEARTS technical package. There is a need to include the perspectives of patients and their families in economic analyses of HEARTS hypertension control programs and account for factors like financing and insurance schemes that impact not only hypertension, but multiple other chronic conditions.

Early results from this ongoing research suggest that hypertension control interventions are cost-effective and the HEARTS hypertension control package is affordable at about \$ 9-\$ 44 per person treated per year and that antihypertensive medicines could be priced low enough to reach a global standard of an average < \$ 5 per patient per year to provide medications alone in the public sector. National scale hypertension programs are dependent on a reliable supply of preferred medicines listed on treatment protocols and optimization of the healthcare workforce via task-sharing and team-based care. Cost-effectiveness and budget impact of HEARTS hypertension control programs are particularly sensitive to medication prices and use of team-based care. Countries considering investment in hypertension control need to provide access to health insurance covering primary health care facility-based HEARTS hypertension services, adopt policies to promote task-sharing and team-based care in primary care, and join in regional and global efforts to control the prices and ensure the quality of antihypertensive medications.

Author contributions. All authors conceived the original idea, contributed descriptions of completed or ongoing research and wrote or reviewed the paper. All authors reviewed and approved the final version of this report.

Funding. AEM, MF, DC, SKS, DM, SA, WI, CA, SRC, SJP, DAW, MJH, KR, KM, MM, DK and RG all receive salary support for their parts of the research described in this review from Resolve to Save Lives, a global non-profit public health organization. Resolve to Save Lives is funded by grants from Bloomberg Philanthropies, the Bill and Melinda Gates Foundation and Gates Philanthropy Partners, which is funded with support from the Chan Zuckerberg Foundation. Support to BH and RN for the study *Evaluating the cost-effectiveness of single pill antihypertensive medicine combination therapy in 24 low- and middle-income countries* work is provided by Cooperative Agreement number 1NU2HGH000044-01-00 funded by the US Centers for Disease Control and Prevention. AP was supported by a Columbia University Global and Population Health intership for the summer of 2021.

Conflicts of interest. None declared.

TABLE 1. Health economics of WHO-HEARTS hypertension control programs in low- and middle-income countries: current active projects

Theme/ Institution	Project name	Co-author leading this work	Countries	Research question	Method	Data sources
HTN program costing						
US CDC	HEARTS costing	D. Kostova	Mexico Chile Bangladesh Thailand Philippines Ethiopia	HEARTS program cost	Mixed methods	Key informants National data observation in facilities
Medicine/ device market research						
Resolve to save lives	Public and private sector antihypertensive drug pricing	D. Cazabon, S. Swahoo	India Brazil South Africa Nigeria Philippines Lebanon	Cost of antihypertensive medicines including SPC vs SAP	Market research	IQVIA State procurements Local pharmacy survey
HTN program budget impact						
University of Washington	University of Washington HEARTS implementation model	D. Watkins, S. Pickersgill	~100 LMIC countries	Health & budget impact	State-transition model	GBD 2019 WHO-CHOICE
HTN program financing redesign						
Johns Hopkins University	Hypertension control program financing	K. Rao	Bangladesh	Optimal blend of financing instruments	Health economics	Literature survey
HTN program services redesign						
Johns Hopkins University	Primary care workforce optimization and supply chain re-design	M. Marklund	India	Optimization of services	Operations research	Literature survey
Research Triangle International (RTI)	Evaluating the impact of single pill combination therapy in LMICs	B. Hutchinson	Africa: Algeria, Kenya, Tanzania, Uganda Americas: Argentina, Brazil, Colombia, Mexico Eastern Mediterranean: Iraq, Libya, Morocco, Sudan Europe: Azerbaijan, Belarus, Kyrgyzstan, Tajikistan South-East Asia: Bangladesh, Myanmar, Nepal, Sri Lanka Western Pacific: Cambodia, Laos, Mongolia, Vietnam	Cost-effectiveness	State-transition model	IHME Epi Visualizations database, STEPS Surveys, WHO HEARTS treatment guidelines, national and international databases, gray and published literature

Source: prepared based on the authors' descriptions of their own studies in progress
 HTN, hypertension; CDC, Centers for Disease Control and Prevention; SPC, single-pill combinations; SAP, single agent pills; LMIC, low- and middle-income countries; GBD, Global Burden of Disease; IHME, Institute for Health Metrics and Evaluation; STEPS, STEPwise approach to NCD risk factor surveillance

TABLE 2. Barriers to adoption of national WHO-HEARTS hypertension control programs and potential solutions provided by health economic analysis

Barrier	Solution
Countries are unlikely to invest budget sufficient to deliver life-long services for a highly prevalent condition like hypertension absent a convincing investment case	Health economic analysis can quantify value for money.
It is hard for countries to finance hypertension control without fundamental improvements to universal access, including health care financing overall. Countries need to explore financing schemes that support a broad package of essential services, including for NCDs but also incentivize highest priority conditions like hypertension.	Health economic modeling may reveal the balance between capitation and disease-specific incentives.
Cost of antihypertensive medications is among the biggest barriers to countries adopting national hypertension control programs, and lack of transparency re drug pricing and variable pricing across countries.	Quantifying cost-effectiveness and budget impact gives countries specific benchmark prices to work toward and may encourage regional or global pooled procurement.
Team-based care is known to be effective compared with usual care, but the economic case for team-based care must be better established. For example, shifting tasks to lower salary healthcare worker cadres should save money; but costing of team-based care complex.	Research is needed to determine what is more important, adding members to the team, or expanding the scope of practice for individual team members.
Presence of a large private sector presence in some countries complicates the design, execution, and health economic evaluation of national hypertension control programs.	Studies in country private sectors are needed, including studies of private sector financial incentives to monitor and retain chronic disease patients, like people living with hypertension.
National health insurance programs may not cover a full package of essential, high-value health care services that includes hypertension screening and treatment.	There is a need for comprehensive and inclusive health services evaluations, including costing and economic analysis of HEARTS hypertension control services in the context of integration with other primary care priority conditions.
A compelling investment case is needed before countries will adopt and scale up the HEARTS hypertension control package must address the needs, incentives, and competing priorities of multiple in-country stakeholders.	Need for regular, intensive engagement of local governments, medication and device manufacturers, health workers, patients and their families, and information system designers in the health economic evaluation process.

Source: This list of barriers and solutions was generated from informal discussion among the authors of this special report.

Disclaimer. Authors hold sole responsibility for the views expressed in the manuscript, which may not necessarily reflect the opinion or policy of the RPSP/PAJPH, the Pan American

Health Organization, the US Centers for Disease Control and Prevention, the US Department of Health and Human Services, The Task Force for Global Health, Inc. or TEPHINET.

REFERENCES

- World Health Organization. Global Action Plan for the Prevention and Control of Non-communicable Diseases, 2013-2020. Geneva: WHO. Available from: <https://www.who.int/publications/i/item/9789241506236>.
- Saving lives, spending less: a strategic response to noncommunicable diseases. Geneva: World Health Organisation; 2018. Available from: <https://apps.who.int/iris/bitstream/handle/10665/272534/WHO-NMH-NVI-18.8-eng.pdf>.
- World Health Organisation. Global Health Expenditure Database. Geneva: WHO; 2021. Available from: <https://apps.who.int/nha/database/Home/Index/en>.
- Institute for Health Metrics and Evaluation. Global Burden of Disease 2019 Results Tool. Seattle: IHME; 2022. Available from: <http://ghdx.healthdata.org/gbd-results-tool>.
- Institute for Health Metrics and Evaluation. Financing Global Health in 2020: the Impact of COVID-19. Seattle: IHME; 2021. Available from: <https://www.healthdata.org/policy-report/financing-global-health-2020-impact-covid-19>.
- Kostova D, Spencer G, Moran AE, Cobb LK, Husain MJ, Datta BK, et al. The cost-effectiveness of hypertension management in low-income and middle-income countries: a review. *BMJ Glob Health*. 2020;5(9).
- Das H, Moran AE, Pathni AK, Sharma B, Kunwar A, Deo S. Cost-Effectiveness of Improved Hypertension Management in India through Increased Treatment Coverage and Adherence: A Mathematical Modeling Study. *Glob Heart*. 2021;16(1):37.
- World Health Organization. HEARTS Technical package for cardiovascular disease management in primary health care. Geneva: WHO; 2016. Available from: <https://apps.who.int/iris/bitstream/handle/10665/252661/9789241511377-eng.pdf?sequence=1>.
- Husain MJ, Datta BK, Kostova D, Joseph KT, Asma S, Richter P, et al. Access to cardiovascular disease and hypertension medicines in developing countries: an analysis of essential medicine Lists, price, availability, and affordability. *J Am Heart Assoc*. 2020;9(9):e015302.
- Resolve to Save Lives. Under Pressure: Strategies to improve access to medicines to treat high blood pressure in low- and middle-income countries. New York: RSL; 2022. Available from: <https://resolvetosavelives.org/assets/Downloads/Docs/RTSL%20Under%20Pressure.pdf>.
- Hill AM, Barber MJ, Gotham D. Estimated costs of production and potential prices for the WHO Essential Medicines List. *BMJ Glob Health*. 2018;3(1):e000571.
- Wang LX, Zahur N. Procurement Institutions and Essential Drug Supply in Low and Middle-Income Countries (March 23, 2022). DOI: <http://dx.doi.org/10.2139/ssrn.3926761>
- Sahoo SK PA, Krishna A, Sharma B, Moran AE, Hering D. Financial implications of protocol-based hypertension treatment: an insight into medication costs in public and private sector health sectors of India. *J Hum Hypertens*. 2022 (forthcoming).
- Negi S, Neupane D, Sahoo SK, Mahajan T, Swaroop K, Moran AE, Sharma B, Pathni AK. Prices of combination medicines and single-molecule antihypertensive medicines in India's private health care sector. *J Clin Hypertens (Greenwich)*. 2021 Apr;23(4):738-743.
- World Health Organization. Guideline for the pharmacological treatment of hypertension in adults. Geneva: WHO; 2021. Available from: <https://www.who.int/publications/i/item/9789240033986>.
- Task Force for Global Health. HEARTS Costing Tool. Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET). Atlanta: Task Force for Global Health; 2022. Available from: <https://www.tephinet.org/tephinet-learning-center/tephinet-library/hearts-costing-tool>.
- Chivardi C, Hutchinson B, Molina V, Moreno E, Fajardo I, Giraldo GP et al. Assessing costs of a hypertension program in primary care:

- evidence from the HEARTS program in Mexico. *Rev Panam Salud Publica*. 2022;46 (forthcoming).
18. Husain MJ, Haider MS, Tarannum R, Jubayer S, Bhuiyan MR, Kostova D, et al. Cost of primary care approaches for hypertension management and risk-based cardiovascular disease prevention in Bangladesh: a HEARTS costing tool application. *BMJ Open*. 2022;12(6):e061467.
 19. Pickersgill SJ WD. The Hypertension Investment Case Tool Seattle: University of Washington; 2022. Available from: <https://dcp-uw.shinyapps.io/HICT/>.
 20. Watkins DA, Qi J, Kawakatsu Y, Pickersgill SJ, Horton SE, Jamison DT. Resource requirements for essential universal health coverage: a modelling study based on findings from Disease Control Priorities, 3rd edition. *Lancet Glob Health*. 2020;8(6):e829-e39.
 21. Etehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet*. 2016;387(10022):957-67.
 22. World Bank. Hypertension and Type-2 Diabetes in Bangladesh: Continuum of Care Assessment and Opportunities for Action. Washington, DC: World Bank; 2019.
 23. Feldhaus I, Mathauer I. Effects of mixed provider payment systems and aligned cost sharing practices on expenditure growth management, efficiency, and equity: a structured review of the literature. *BMC Health Serv Res*. 2018;18(1):996.
 24. Nguyen TP, Wright EP, Nguyen TT, Schuiling-Veninga CC, Bijlsma MJ, Nguyen TB, et al. Cost-Effectiveness Analysis of Screening for and Managing Identified Hypertension for Cardiovascular Disease Prevention in Vietnam. *PLoS One*. 2016;11(5):e0155699.
 25. Bruyn E, Nguyen L, Schutte AE, Murphy A, Perel P, Webster R. Implementing Single-Pill Combination Therapy for Hypertension: A Scoping Review of Key Health System Requirements in 30 Low- and Middle-Income Countries. *Glob Heart*. 2022;17(1):6.
 26. Parati G, Kjeldsen S, Coca A, Cushman WC, Wang J. Adherence to Single-Pill Versus Free-Equivalent Combination Therapy in Hypertension: A Systematic Review and Meta-Analysis. *Hypertension*. 2021;77(2):692-705.
 27. Wald DS, Law M, Morris JK, Bestwick JP, Wald NJ. Combination therapy versus monotherapy in reducing blood pressure: meta-analysis on 11,000 participants from 42 trials. *Am J Med*. 2009;122(3):290-300.

Manuscript submitted on 28 March 2022. Revised version accepted for publication on 11 July 2022.

Argumentos de la economía de la salud para ampliar las medidas de control de la hipertensión de la iniciativa HEARTS de la OMS en los países de ingresos medianos y bajos

RESUMEN

En general, los programas de control de la hipertensión son costo-eficaces, incluso en los países de ingresos bajos y medios. Aun así, es poco probable que los gobiernos nacionales y la sociedad civil apoyen los programas de control de la hipertensión a menos que se demuestre su valor en términos de beneficios para la salud pública, impacto presupuestario y valor de la inversión para el contexto individual del país. La Organización Mundial de la Salud (OMS) y la Organización Panamericana de la Salud (OPS) implementaron la iniciativa HEARTS, un enfoque mundial estandarizado y simplificado para el control de la hipertensión, que incluye los medicamentos antihipertensivos y los dispositivos de medición de la presión arterial de preferencia. El objetivo de este estudio es informar sobre los estudios en el ámbito de la economía de la salud relativos al costo de las medidas de control de la hipertensión previstas en HEARTS (especialmente, de los medicamentos), la costo-efectividad y el impacto presupuestario, así como describir los modelos matemáticos diseñados para traducir los datos de este programa en un enfoque óptimo para la prestación y el financiamiento de los servicios de atención de la hipertensión, especialmente en países de ingresos medianos y bajos. Los primeros resultados indican que las intervenciones de HEARTS para el control de la hipertensión son de bajo costo o costo-eficaces, que el conjunto de medidas HEARTS es asequible, a un precio que oscila entre US\$ 18 y US\$ 44 al año por paciente tratado, y que los medicamentos antihipertensivos podrían tener un precio lo suficientemente bajo como para alcanzar un estándar medio mundial de <US\$ 5 por paciente al año en el sector público. Estos datos del ámbito de la economía de la salud serán argumentos convincentes para que los gobiernos se involucren en los programas de control de la hipertensión a escala nacional y les brinden apoyo financiero.

Palabras clave

Accesibilidad a los servicios de salud; análisis costo-beneficio; hipertensión; enfermedades cardiovasculares.

Ampliação do pacote de controle da hipertensão OMS-HEARTS em países de baixa e média renda: argumentos a partir da perspectiva da economia em saúde

RESUMO

Geralmente, os programas de controle de hipertensão são custo-efetivos, inclusive em países de baixa e média renda, mas os governos dos países e a sociedade civil provavelmente não apoiarão tais programas a menos que demonstrem valor em termos de benefícios à saúde pública, impacto orçamentário e retorno sobre o investimento no contexto individual do país. A Organização Mundial da Saúde (OMS) e a Organização Pan-Americana da Saúde (OPAS) criaram a Global HEARTS, uma abordagem padrão e simplificada ao controle da hipertensão arterial, que inclui medicamentos anti-hipertensivos preferidos e dispositivos para aferição da pressão arterial preferidos. O objetivo deste estudo é relatar os estudos de economia em saúde que analisaram o custo (especialmente custos de medicamentos), custo-benefício e impacto orçamentário do pacote HEARTS para controle da hipertensão e descrever modelos matemáticos elaborados para traduzir os dados do programa de controle de hipertensão em uma abordagem ideal para a prestação e financiamento de serviços de atenção às pessoas com hipertensão, especialmente em países de baixa e média renda. Os primeiros resultados sugerem que as intervenções HEARTS para controle da hipertensão são de baixo custo ou custo-efetivas, que o pacote HEARTS é acessível (custando de US\$ 18 a 44 por pessoa tratada por ano) e que o preço dos medicamentos anti-hipertensivos poderia ser baixo o suficiente para atingir uma média global de <US\$ 18 por paciente por ano no setor público. Estas evidências do campo da economia em saúde serão um argumento convincente para que os governos se responsabilizem por programas de controle de hipertensão em escala nacional e os dotem de recursos financeiros.

Palavras-chave Acesso aos serviços de saúde; análise custo-benefício; hipertensão; doenças cardiovasculares.
